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The Eye as the Portal of Entry of Infections

by

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Approach to the Concept

My approach to the discovery that the route of infection in certain diseases is across the intact conjunctiva, was a sequel to many years of observation and experiment on the transmission of infection and on immunity in measles. In 1920 we began to use convalescent serum in our wards with great success in the prophylaxis of measles in contacts. While this was recognized to be a considerable advance, it was evident that the problem of measles as a whole could not be solved without some practical form of active immunization.

Accordingly, I attempted, in 1920, to inoculate the disease by subcutaneous injection of 0·1 ml. of a 1:10 dilution of blood from a case of measles in the early acute stage. [Here I was following the lead of my countryman, M. KATONA, who, in 1843, had inoculated the disease by applying measles blood to the scarified skin, on the analogy of the practice of variolization for smallpox in the 18th century.] I was thus able, like Katona, to produce a modified form of measles with an incubation period 4 days shorter than that of the natural infection. In 1925, working in Paris with Professor R. DEBRÉ (Debré *et al.* 1926, 1928) I continued and extended these experiments. By means of a course of inoculations of highly diluted blood from patients, 1:800, 1:400, and 1:200, given at intervals of 4 weeks, we were able to produce a long-lasting active immunity in over 2,000 children, as shown by follow-up enquiries in succeeding years, and in most cases without causing any symptoms. It was clear from these experiments that the measles virus is present in high concentration in the blood of patients in the early acute stage of measles.

Attempts at infection via the upper respiratory tract

In 1933 I was able to show, by differential centrifugation of blood from early cases of measles, that the virus was contained in the leucocyte layer, and not, in infective quantities at least, in the serum or plasma (Papp, 1933, 1937a). I now used virus-infected leucocytes as the infected material, and during the next few years tried many times, and repeatedly on the same persons, to reproduce measles by swabbing infected leucocytes on the mucous membranes of the upper respiratory tract; with this method I had no success whatever. I reported these failures at the Paediatric Congress in Rome in 1937 (Papp, 1937b), and about this time began to think of the eye as a possible portal of entry of infection. Indeed, in August 1937 I instilled a minute quantity of highly diluted measles saliva into the conjunctival sacs of a 10-year-old girl, and a modified attack of measles followed after the regular incubation period. However, this child had not been kept under control, and I considered at the time that the measles had probably been a natural infection.

About this time my attention was diverted from the eye by the work of C. HERRMAN of New York in producing passive-active immunity against measles in babies about 5 months old; he did this by inoculating them with infective material at the time when their passive immunity, inherited from the mother, was waning (Herrman, 1923, 1929). During the next 6 years, by modification of Herrman's method, I succeeded in producing lasting immunity in about 1800 babies, without the occurrence of symptoms of measles; the method was to give them, at spaced intervals and at the appropriate age, 2 or 3 subcutaneous injections of measles-infected leucocytes (Papp, 1940a and b; 1943). Many of these children have been followed up to the age of 15–20 years and still appear to be immune.

The role of the blood circulation of the eye

In 1943 F. KISS, Professor of anatomy in Budapest, called my attention to a peculiarity in the capillary circulation of the eye which seemed to have a bearing on absorption through the conjunctiva. The superficial capillary system of the conjunctiva is a very fine plexus draining by relatively wide vessels into a much coarser deep plexus; in this system a suction effect can be observed which seems to result partly from this sudden widening of the vessels draining the fine capillaries, and partly from the *vis a tergo* produced by the intermittent negative pressure in the venous return to the heart (Kiss and Orbán, 1951).

Experimental Infection via the Conjunctiva

This information suddenly suggested to me a possible explanation of my success in 1937 with inoculation of measles into the conjunctival sac. I immediately continued such experiments, controlling them by similar applications of infected material to the mucous membrane of the upper respiratory passages. Very favourable results were obtained by swabbing the eyes with highly diluted infected saliva from measles, mumps, and rubella, but absolutely negative results when similar infective material was painted on the upper respiratory mucous membranes. For example, measles was transmitted across the intact conjunctiva in 5 out of 6 susceptible children by means of saliva taken from cases of measles in the first 3 days of eruption. On the other hand, no result was obtained in 9 susceptible children whose buccal mucosa and tonsils were painted with diluted infective measles saliva; and only 2 out of 13 such children developed measles when the infective saliva was instilled into the nose. With the same eye technique in mumps 2 positive results in 10 trials were reported, but failure resulted in 6 cases out of 6 when the infective mumps saliva was painted on the buccal mucosa and tonsils. Rubella was similarly transmitted across the conjunctiva in 2 cases out of 6; but no success was obtained with chickenpox transmission in 21 instances, both saliva and fluid from vesicles being used (Papp, 1954). These results were so clear-cut that I had to seek an explanation for the success of ANDERSON (1949) in transmitting rubella by infectious material sprayed into the mouth. It seemed to me that in Anderson's experiments the infection may have reached the eyes as well as the mouth. That the virus was present in the air of the laboratory is shown by the fact that a laboratory assistant who entered the room while spraying was being done, and stood some distance off, contracted rubella at the same time as the volunteers. Thus, in order to prove infection by the upper respiratory passages when the method of spraying is used, the eyes should be closely sealed off.

The Eye as the Sole Portal of Entry of Infection

The important question then arose whether the eye was merely one, or the sole, portal of entry in certain infections. A clear answer, as far as measles is concerned, was obtained by two types of experiments. (1) Each of 3 groups of 3 non-immune children wearing goggles closely sealed to the face, were brought into contact for a few minutes with a highly infective patient in the catarrhal stage of measles, and none of these children developed measles (Papp, 1956). (2) Over 800 non-immune children under the care of various physicians in Hungary (*e.g.* G. RUSTI (1957)) and in Yugoslavia (JOVANOVIC, 1958), have now been exposed to the infections of measles, mumps, rubella, and chickenpox, and with few exceptions have been prevented from contracting these infections by the timely instillation of one drop of the appropriate convalescent serum in each eye. In the case of measles, the disease was prevented when the instillation was made within 15 hours of exposure to infection, but if it was delayed up to 24 hours after exposure, a modified form of the disease was the usual result, although the disease might be unmodified. This series of children now includes 347 contacts of measles, 354 of mumps, 12 of rubella, and 157 of chickenpox (Papp, 1957). As regards chickenpox I must re-emphasize that I have not yet succeeded in inoculating varicella virus through the eye, and Rusti's apparent success in the prophylaxis of chickenpox by conjunctival instillation of convalescent serum remains at present unexplained. As regards mumps, D. Jovanović (1958) has shown in Novi Sad, Yugoslavia, that, following its introduction into a children's (or other closed) community, the convalescent serum should be instilled into the eyes of contacts on the 13th to 19th day after appearance of the first case, and again after the first case of the second wave of infections. This will generally stop all succeeding waves of the infection and so bring the outbreak to an abrupt close. In the case of chickenpox he adopts a similar procedure to stop the infection after the first wave; he inoculates the eyes of contacts on the 16th, 17th and 18th day after exposure to infection, and isolates immediately on the top floor any cases which develop chickenpox. This type of work has not only produced evidence that infection in these diseases can be stopped at its portal of entry—the eye, but has also provided a new and highly economical way of employing convalescent serum in the prophylaxis of these infections.

Other Evidence on the Importance of Conjunctival Infection

In England an important controlled experiment on the eye as a portal of entry of salmonella infection in laboratory guineapigs, was carried out by MOORE (1957). During an epizootic, a group of the animals protected by sealed-off goggles suffered far less infection than a control group of un-goggled animals; and it was actually easier to recover the causative organism, *Salmonella enteritidis*, by swabbing the eyes than by swabbing the rectum. A brief survey of the current evidence for infection across the intact conjunctiva was published by Banks (1958). More recently, HANNOUN (1959) has shown that a conjunctival instillation of active influenza A virus (PR8 strain) produces high titres of antibodies in rabbits. The amount of virus required by instillation is always lower than that required by parenteral inoculation to produce the same result. Inactivated virus instilled conjunctivally, on the other hand, possesses a very low immunizing capacity. It would therefore seem that the live virus must be absorbed from the eye to undergo active multiplication, although the rabbits do not manifest any symptom or lesion.

A. TERRAGNA (1959) has confirmed the importance of the conjunctival route of infection in measles, but cannot yet agree that it is the sole route of infection. In the following experiments he had no failures:

(1) The eyes of 4 susceptible children were swabbed with infective naso-pharyngeal mucus, and all contracted measles after an incubation period of 9–14 days.

(2) 4 susceptible children had their eyes completely protected by an accurately fitting bandage, and were exposed daily for a few hours during 7 to 9 consecutive days to patients in the prodromal and eruptive phases of measles; they were then kept in isolation during an

observation period of 40 to 60 days, and none developed measles.

(3) 12 children were exposed to acute measles, and within 12–24 hours of this exposure, had one drop of convalescent serum put into their conjunctival sacs; the instillation was repeated daily for several days and they were kept in strict isolation. None developed measles within the normal incubation period, although 1 had an attack after 28 days—probably from a different source of infection.

The rapidity of absorption of infection from the conjunctival surface was recently demonstrated by SERENY (1957). He produced in guineapigs a well-defined keratoconjunctivitis as a model disease for the study of dysentery, by swabbing their conjunctiva with *Shigella flexneri*, 10 million to each eye. In the course of these experiments he endeavoured to wash the bacilli out of the eyes of 6 guineapigs with 350 ml. physiological saline solution one minute after swabbing; in both the eyes of all these animals typical keratoconjunctivitis shigellosa developed, and agglutinins as well as mouse-protective antibodies were demonstrated. This experiment appears to support Kiss's theory of a rapidly-acting suction effect on fluid absorbed into the fine capillary circulation of the conjunctiva.

Conclusion

Thus in certain of the common virus infectious diseases, as well as in some bacterial infections, there is clear evidence that the eye is the principal, and may be the sole, normal portal of entry of the infection.

I have to acknowledge with deep gratitude the valuable help received from Dr. H. Stanley BANKS in the presentation of the text of this article in English.

Summary

1. The virus of measles is present in infective amounts in the leucocytes of the blood stream in the early acute stage of measles.
2. Infected leucocytes and saliva were swabbed on the mucous membranes of the upper respiratory tract of susceptible children on many occasions, but no success was obtained in the transmission of the disease.
3. By contrast very favourable results in transmission of measles, mumps, and rubella, were obtained when the same highly diluted materials were swabbed on the conjunctivae of susceptible children.
4. Susceptible children wearing closely-fitting sealed-off goggles can be intimately exposed to measles infection without contracting the disease.
5. Timely instillation of one drop of the appropriate convalescent serum in each eye of susceptible contacts is an effective and economical method of prophylaxis in measles contacts, and probably also in contacts of mumps and rubella.
6. The eye is an important portal of entry of the measles virus and probably also of some other viral and bacterial infections.

References

ANDERSON, S. G. (1949), *J. Immunology*, v. 62, 29. [*Bull. Hyg.*, 1949, 927.]
BANKS, H. S. (1958), *Lancet*, v. 2, 518. [*Bull. Hyg.*, 1959, 187.]
DEBRÉ, R., JOANNON, P., PAPP, K. (1926), *Ann. de Méd.*, v. 20, 343. [*Bull. Hyg.*, 1927, 284.]
——, PAPP, K. *et al.* (1928), *ibid.*, v. 23, 119. [*Bull. Hyg.*, 1928, 696.]
HANNOUN, C. (1959), *Ann. Inst. Pasteur*, v. 96, 170. [*Bull. Hyg.*, 1959, 686.]
HERRMAN, C. (1923), *New York State J. of Med.*, v. 23, 404.
—— (1929), *ibid.*, v. 29, 202.
JOVANOVIĆ, D. (1958), *Medicinski Glasnik*, Belgrade, v. 12, 118.
KATONA, M. (1843), *Gazette Méd.*, Paris, 401.
KISS, F., ORBÁN, T. (1951), *Acta Morphologica*, Budapest, v. 1, fasc. 1, 23.
MOORE, B. (1957), *J. Hygiene*, v. 55, 414. [*Bull. Hyg.*, 1958, 163.]
PAPP, K. (1933), *Acta Paediatrica*, Uppsala, v. 16, 408.
—— (1937a), *Bull. Acad. de Méd.*, v. 117, 46.
—— (1937b), *Acta Paediatrica*, Uppsala, v. 22, 406.
—— (1940a), *Orvostudományi Közlemények*, Budapest, No. 9, 260.
—— (1940b), *Anya-és Csecsemövédelem*, Budapest, v. 13, 371.
—— (1943), *Orvostudományi Közlemények*, Budapest, No. 12.
—— (1954), *Rev. d'Immunologie*, v. 18, 380. [*Bull. Hyg.*, 1955, 941.]
—— (1956), *ibid.*, v. 20, 27. [*Bull. Hyg.*, 1956, 985.]
—— (1957), *Arch. Françaises de Pédiatrie*, v. 14, 1049, 1053.
RUSTI, J. (1957), *Rev. d'Immunologie*, v. 21, 393. [*Bull. Hyg.*, 1958, 813.]
SERENY, B. (1957), *Acta Microbiologica*, Budapest, v. 4, 367. [*Bull. Hyg.*, 1958, 690.]
TERRAGNA, A. (1959), *Giorn. di Malattie Infettive et Parassit.*, 1959, v. 11, 293. [*Bull. Hyg.*, 1959, 983.]

Public Health

SCOTLAND. **Report of the Department of Health for Scotland 1958** [ANDERSON, J., Secretary]. Cmnd. 697. 111 pp. 1959. London: H.M. Stationery Office. [5s. 6d.]

This annual report covers for Scotland the whole field of health and sanitary endeavour. The format is similar to that of the report for 1957 [this *Bulletin*, 1958, v. 33, 809].

"The general trends . . . continue to be favourable." There are further improvements in the infant mortality and those from tuberculosis and other infectious diseases. Adverse factors are the rising mortality from cancer of the lung, the high incidence of bronchitis and the death-rate from coronary atherosclerosis. There are special sections on each of these as well as on atmospheric pollution and on the care of the aged. The 2-year mass radiography campaign has been successfully completed.

A good feature of the Scottish report has been its early appearance. This one is dated 31 March but in future there will be longer delay as it has been decided to await the completion of the vital statistics for the year reported upon instead of using the few provisional figures available in the early months of the following year.

The mental health section points out that the admission of voluntary short-stay patients is increasing but that the number of patients resident in mental hospitals remains fairly constant: 80% of them suffer from severe mental disorder and remain for long periods: over 7,000 had been there for over 15 years.

Cancer causes 17% of all deaths: there is now a universal record system for cancer cases in all hospitals and it is estimated that there are about 25,000 new cases each year.

Much attention is paid to maternal and child welfare and statistics for this section are available and have never been better. The rate of infant mortality was 27·7 and the neonatal mortality 18·7 per 1,000 live births: the stillbirth rate 22·8 and the perinatal mortality 41·5 per 1,000 total births. The maternal mortality was 0·5 per 1,000 births. The local authorities provided 10 new maternity and child welfare centres during the year.

The incidence of poliomyelitis was about double that of 1957. There was no recurrence of influenza. There was little diphtheria and whooping cough was not nearly so prevalent. Dysentery of a mild type was troublesome and gonorrhoea is becoming more prevalent.

Dental caries is widespread and there is a shortage of dentists. "The former attention to malnutrition will have to shift to the problems of overfeeding."

50% of the adult population have had their chests X-rayed in the past 2 years. School leavers are tested with tuberculin: 27% gave positive reactions compared with 66% in 1952: 726 beds for respiratory tuberculosis have become available for other purposes: 3 industrial chest disease centres have been opened.

The hospital service cost £42,967,469 and provided 63,950 beds. In addition capital expenditure on buildings and equipment amounted to £3,200,000. There were 2 serious outbreaks of staphylococcal infection in maternity hospitals and it is suggested that every major hospital should have an "Infection Control Officer". Fatal burns are proportionately higher in Scotland than in England: there were 96 deaths and for every fatal case about 9 others are seriously injured.

Scotland has always recognized the value of medical administration in hospitals and in order to give better career prospects to medical administrators the medical administrative staffs of the Regional Hospital Boards have been amalgamated with the non-clinical medical superintendents of hospitals.

The hospitals have been urged to develop schemes for rehabilitation and for the care of the aged.

The number of doctors working in the Scottish health service has increased by 24 to 5,668 (2,764 in hospitals, 286 in the local authority service and 2,618 in the general medical service). Nurses and midwives of all grades increased by 513 during the year and now number 30,794. There is a better distribution of doctors in the general medical service: in 1949 there were 49 under-doctored areas; in 1958 only 17.

At mid-year there were 6,971 persons in Welfare Homes. New houses completed during the year numbered 32,170 and 12,232 slum dwellings were demolished or closed.

£7·1m. capital were spent on water supplies, sewage disposal and other services of a sanitary nature.

The report is a splendid record of a good year's work where there is wisdom to evaluate old procedures and courage to change or scrap them whenever needed. The department keeps abreast of modern thought and is forward-looking in its policy. *Allen Daley*

MINISTRY OF HEALTH. DEPT. OF HEALTH FOR SCOTLAND. **Report of the Working Party on Social Workers in the Local Authority Health and Welfare Services.** [YOUNGHUSBAND, EILEEN L. (C.B.E., LL.D., J.P.), Chairman]. pp. xi + 375. 1959. London: H.M. Stationery Office. [15s.]

This comprehensive report is a sequel to that of the Working Party on Health Visitors [this *Bulletin*, 1957, v. 32, 4] where it was stated "The Health Visitor may herself be able to deal satisfactorily by way of advice with many of the family welfare problems that she meets. In a substantial number of cases she will be handicapped by lack of time" . . . or the problem may be beyond her ability to identify fully or deal with".

This working party had 10 members under the chairmanship of a distinguished teacher of the social sciences; the vice-chairman is in the same field of work; there were 3 other social workers; including one from the National Association for Mental Health; 2 doctors, one of them a medical officer of health; a principal welfare officer; an education officer and a county clerk. They have spent 4 years on their task and have accumulated a vast and unique array of facts from which it is clear that the range and amount of social work needed to fulfil the varied functions of local authorities are immense. The number of people and of voluntary

bodies engaged in social work is already so vast that it has been found necessary to devote a chapter of the report to the methods adopted to ensure cooperation and some coordination of their work. The report recommends that even more should be employed.

The main groups of social workers now in the service of local authorities are welfare officers under the National Assistance Act, visitors to the handicapped, home teachers of the blind and workers with the deaf, mental welfare officers, other social workers in health departments concerned with family problems, such as unmarried mothers, and in the social aspects of the after-care service. Few have had general training in social science and many have acquired their knowledge of the work solely by working "on the job". It is recommended that "professionally trained and experienced social workers should provide a casework service and generally advise and help other staff in dealing with difficult cases in a range of services. They should supervise newly qualified or appointed social workers and assist with in-service training". In addition to those listed above there are social workers employed in several other departments of local government work as well as in departments of central government such as the National Assistance Board and the Ministry of Pensions and National Insurance.

A function of a local authority social worker should be "to assess the disturbance of equilibrium in a given handicapped person and in his family and social relationships so as to give appropriate help". Another is "to help the individual to achieve the best possible personal, family and social adjustment". Further, social workers should assume for the socially inadequate "responsibilities beyond their (*i.e.* the families') capacity to shoulder". These are fine words and desirable objectives which the Working Party hope can be attained if their recommendations are implemented.

Great importance is attached to casework of which a long definition is given.

It is quite rightly stated that there are too many specialists, each working in a narrow and limited field. It is recommended that there is need for a "general purpose social worker" though they think that a better title would be "qualified social worker".

The social needs of individuals are of 3 degrees of complexity: (a) straightforward, (b) more complex, and (c) of special difficulty. To cope with them people of increasing training and experience are required. For (a) a new type of worker with a short but systematically planned in-service training should suffice; for (b) a social worker with 2 years' full-time training or its equivalent is needed and for (c) a professionally trained and experienced social worker such as a psychiatric social worker, an almoner or a family care worker. The third group need a basic training in social science followed by a professional training in social work.

Estimates are provided of the numbers required in each category and suggestions made about how their work should interlock with that of other workers in cognate fields. A National Council for Social Work Training is proposed to approve training courses and maintain examination and other standards. The cost of implementing their proposals is admitted to be high but if they bring about the desired results there would be some compensating savings. There is mention of the need for better record keeping on which research could be based and of the desirability of a national staff college.

The zeal with which the facts have been collected, analysed and presented arouses nothing but admiration, but with regard to their recommendations it is only realistic to point out that local authorities are hard-headed and that they will need much convincing before they guarantee permanent employment for the large number of additional staff envisaged. But it is to be hoped that this report will not share the fate of several other reports of working parties, for example that recommending a 2-year basic training course for nurses, which still gather dust on the blook shelves.

There are recommendations on such urgent matters as the need for training mental health workers and this might be considered forthwith despite the injunction in the report that all their proposals are interrelated and none can be taken out and dealt with piecemeal.

Allen Daley

CHOONG AH KONG. **Some Aspects of Health and Environment in Rural Malaya.** *Sanitarian.* London. 1959, May, v. 67, No. 8, 371–80.

This paper describes the rural health services in Malaya, comments on their defects and suggests remedies. It points out that while urban health has been considerably improved, in rural areas health services are grossly inadequate and may be deteriorating. Though the emphasis is still on curative medicine, rural health has become a political issue since World War II and the Emergency in Malaya, and a rural health service has been established. In areas outside the municipalities this service is responsible for all health matters except environmental hygiene which is the responsibility of the local councils. The latter do not employ medical officers of health, and only in a few instances do they have public health inspectors. Health workers consider that in present conditions environmental hygiene should be a function of central government. The country's advancement depends on the economic and social progress of its rural people and the nationalist movement demands improved living conditions for the masses. Population pressure is becoming a problem; the 1957 census indicates a probable doubling of population in 25 years without taking into account a lowering of the infant mortality or an increase in life expectancy. It is doubtful whether the present standard of living can be maintained with such a rapid expansion.

The paper then describes the environment of a Malayan kampong and the new villages built for the Chinese during the emergency. The kampong, which is a very spread-out village, is without hygienic facilities but risk of spread of disease is low owing to population dispersal. The villages being concentrated have a higher disease risk because they do not use the protected wells and sanitary disposal systems which have been provided. The paper then comments on certain aspects of hygiene in rural areas of Malaya, dealing with disease incidence, nutrition, housing, water supplies, scavenging and conservancy, health education and training of health workers.

T. H. Davey

GOLUBEV, A. **On the Methods for establishing the Requirements regarding Medical Staffs in the U.S.S.R.** *Santé Publique.* Bucharest. 1958, v. 1, No. 1, 21–39.

This long paper purports to describe how the U.S.S.R. calculates how many doctors it needs. The figures are prepared yearly in each State and worked up into a balanced 5-year plan for the whole U.S.S.R.

The aim is to provide complete cover for both preventive and curative medicine and to staff teaching institutions and research establishments.

The first step is to consider whether existing medical institutions are adequate and if not how many more of each type are needed, where they should be located, what they will cost and the availability of the money. Standards for buildings and equipment are available centrally and any new construction must be sanctioned by the State Planning Boards.

The U.S.S.R. contains 15 republics each with its own national peculiarities and differences in the factors which affect medical staffing, such as population density, birth rate and the incidence of disease. Staffing standards have been devised for towns but not yet for rural areas. Data are needed to show the existing number and the distribution of the doctors, the ratio per 10,000 population, what increase in the ratio is likely to be needed and the number of students in training. Figures are also required to show the ratio between established posts and the number actually filled and the extent to which an individual fills more than 1 post. Separate calculations are needed for the different specialties and types of medical and paramedical workers. The working papers must show the number of domiciliary visits from the polyclinics, the number of hospital beds and the annual turnover of patients in them. Another factor is the length of the doctor's working day which may be 4, 5 or 6 hours and the number of days he works each year, which varies from 283 to 289.

The optimum staffing standard for "curative-prophylactic assistance" is about 30–31 medical officers per 10,000 inhabitants in towns and in rural areas, where some of the work is done by "feldschers" and some is sent to towns, about 12–13.

In the U.S.S.R. all the young children of working mothers are sent to nurseries: the average staffing ratios for paediatricians are 1·5 per 100 places in an urban day nursery, 1 in a rural and 3·5 in a residential.

For epidemiology and sanitation no firm standards are possible but in towns there are 2·7–2·8 positions and in rural areas 0·4 per 10,000 population.

Research and teaching institutions have 3·2 positions per 10,000 population.

A national figure is built up from all these components and losses due to illness, death, age or change of occupation are estimated. *Allen Daley*

STEUART, G. **The Importance of Programme Planning.** *Internat. J. Health Education.* Geneva. 1959, Apr., v. 2, No. 2, 94–100.

It is a common fallacy that detailed planning is not a part of a community health programme and that it merely delays action. In consequence many such programmes suffer. The author of this paper claims that planning is not just a prelude but has an important educational function. It has 3 interdependent aspects: the definition of objectives, the design of programme evaluation, and the determination of methods to achieve these ends. The objectives must be desired both by the health staff and the people, and they must be stated in a form that is measurable by both parties. It is emphasized that the community is not just a passively receptive aggregate of people, but is a dynamic network of human relationships and communication channels. Since it is self-educating the selection of individuals and groups to influence is as vital a decision as choosing direction in which they should be guided.

To illustrate these principles the author describes the health education aspects of an antenatal and maternity programme undertaken in Durban. The planning procedures are described in considerable detail from the first consideration of the programme up to the trial runs and final launching of the campaign. Those who are concerned with health education will find this article full of sound advice as to how they should set about planning their campaign once the broad objectives have been decided. *T. H. Davey*

Maternal and Child Health

DEPT. OF HEALTH FOR SCOTLAND: SCOTTISH HEALTH SERVICES COUNCIL. **Maternity Services in Scotland.** Report by a Committee [MONTGOMERY, G. L., Chairman] appointed by the Council. 64 pp. 1959. Edinburgh: H.M. Stationery Office. [3s. 6d.]

This exceptionally well-written report is the Scottish counterpart of the Cranbrook Committee's report [this *Bulletin*, 1959, v. 34, 598]. The 17 members included 9 doctors and 3 midwives: 7 were women.

The Scottish maternity services have the same broad outline as the English but they differ in detail: for example, the Maternity Services (Scotland) Act, 1937 required local authorities in Scotland to provide not only the services of a midwife, as in England, but also those of a general medical practitioner, and when required a specialist obstetrician and anaesthetic help. Another important difference is that there has been no selected list of general-practitioner-obstetricians in Scotland as there has been since 1948 in England.

The presentation of the report is particularly good.

There is a good summary of the evidence received, a discussion of a number of controversial points and, finally, a short summary of recommendations.

Maternity work must be organized as a single service despite the fact that there are many choices and many components such as midwives, general practitioners, specialist obstetricians, the ambulance service, hospital officers, local authorities (the MOH), health visitors, the supervisor of midwives, and ante-natal and post-natal clinics.

The general impression given by the evidence is that the existing framework is sound as is shown by the fact that in some areas excellent coordination has been achieved. But it is disclosed that this is by no means universal.

"We think that a primary requirement is that one person should be regarded as the co-ordinator" and it is suggested that he should be the general medical practitioner to whom the fact that one of his patients is pregnant should be reported by the person whom she engages to conduct her confinement.

To ensure that liaison receives adequate attention at the administrative level each of the 5 Hospital Boards should be required to prepare a report setting out the arrangements for coordination in operation and the method of maintaining them. Also, the Scottish Health Services Council should set up a Standing Advisory Committee on the Maternity Services.

At the patients' level it should be the responsibility of the general practitioner to provide or secure the provision of all the facilities required by the mother during pregnancy, confinement or lying-in.

A controversial recommendation is that the English example should be followed and a list of general-practitioner-obstetricians established. At present, any registered medical practitioner in Scotland can elect to go on the list of those willing to provide maternity services and 2,418 out of the 2,575 on the general medical list have so elected though 21% of them have not been called upon to undertake midwifery. Any doctor on the present self-selected maternity services list should be accepted on the new list but new entrants will be limited to those who have held a 6-months' resident post in an obstetric unit. For all, a condition for retention on the list is that a refresher course be attended not less often than every 5 years.

Much space is devoted to hospital confinement. The percentage varies in different local authority areas between 50·4 and 96·4 with a national average of about 70. A table shows the number of additional beds needed in each hospital region to provide for 70, 75 and 80% of the births together with 8 beds per 1,000 births for ante-natal admissions. For 75% plus the ante-natal beds, 687 new beds would be required for Scotland and the cost would be about £5,000 a bed though it should be cheaper if the new beds are in general practitioner hospitals or units as is suggested.

An interesting table compares the cost to public funds of domiciliary and hospital confinement and the difference in favour of home confinement is not so large as was once thought. The shortage of beds is most marked in the Western Hospital Region (Glasgow). Whenever beds are in short supply it is essential that the best use be made of them. The priorities are discussed and suggestions made. Provisional bookings and sending patients home before the tenth day are deprecated.

The educational work of local authority ante-natal clinics is commended and it is recommended that the clinic premises and the services of their staff should be utilized both by the hospitals and by the general practitioner-obstetricians. The medical staffing of local authority ante-natal clinics should no longer be in the hands of doctors with no responsibility for attending confinements.

There is an interesting section on why it is considered inadvisable for any central body to try to devise a "code of practice" for distribution to the professional people concerned. It is, also, not recommended that a national standard form of record be introduced.

Maternal mortality in Scotland has declined from 6·13 per 1,000 births, live and still, in 1931–5 to 0·45 in 1955 and 0·5 in 1956. In 1956 the live births numbered 95,313 and the stillbirths 2,329. The stillbirth rate was 23·9 and the neonatal mortality 19·1. *Allen Daley*

RÄIHÄ, C. E. Prematuritet. Betydelse och försök till profylax. **[Prematurity. Importance and Attempts at Prevention]** *Nordisk Med.* 1959, May 28, v. 61, No. 22, 819–23, 5 figs. [30 refs.]

The English summary appended to the paper is as follows:—

"The paediatric concept 'a premature baby' does not always correspond to the biological age or to maturity and viability, but it is suitable for statistical and clinical purposes. The perinatal mortality, being about 3.5 per cent, consists of more than 50 per cent of prematures. Every fourth patient with cerebral palsy is a premature, as are 25 per cent of the patients who need lifelong institutional care because of cerebral palsy, epilepsy or oligophrenia. The aetiology of prematurity is discussed and it is postulated that the working capacity of the pregnant woman in relation to the demand of work is an important factor which determines the birth weight of the child and the duration of pregnancy. The working capacity can be objectively estimated by measuring the heart volume using X-ray in two dimensions. There is a significant correlation between the heart volume of the pregnant woman and the birth weight of the baby, and also between the heart volume and the risk of premature birth. By advising mothers who had a heart volume below 320 cc per square metre of body surface to avoid heavy work and to rest for some hours every day, the frequency of prematures was reduced to 2.4 per cent, with only 3 prematures with a birth weight below 2,000 g, out of a total of 20. The perinatal mortality fell to 1.6 per cent. Among 797 cases there were 8 stillbirths and 5 deaths during the first week of life."

BELLOC, Nedra B., MATTSON, Phyllis H. & SIMMONS, W. D. **Blindness in California Children.** *Pub. Health Rep.* Wash. 1959, May, v. 74, No. 5, 444–8.

In collecting data for this survey of blindness in children in California in 1956 efforts were made to

make it as comprehensive as possible, but for various reasons some sources of information had to be excluded. The survey covers a total of 1,338 blind children of whom 568 were under the age of 6 and 770 between 6 and 17. Blindness is here defined as visual acuity of 20/200 or less in the better eye with maximum correction.

The rate of blindness was calculated to be 33 per 100,000 children which is considerably higher than those recorded in previous studies. High rates of over 40 were found in children 2, 3 and 4 years of age and were due to the prevalence of retrolental fibroplasia. The incidence of this condition has been reduced drastically since 1956 because of the control measures which were introduced after it was discovered to be due to the use of excessive oxygen for newborn premature infants.

The data on blindness were analysed by cause and type of eye disorder and tables set out the numbers of blind children by age, the school status of the children and handicapping conditions which existed in addition to the blindness. The most common cause was retinal disorders, of which there were 632 cases—438 in children under 5 and 194 in the 6–17-year group. "Congenital conditions made up the next largest group, accounting for 14 per cent of the preschool group and nearly half of those in the older age group." The total of these was 455 and as they are primarily of unknown origin a "substantial reduction in the number of blind children in future years can only be achieved through the determination of ways to prevent these conditions".

M. E. Delafield

FLORENTIN, Miriam. **A Survey of Vitamin Intake in Infancy.** *Med. Officer.* 1959, Jan. 2, v. 101, No. 1, 5.

Most dried milks and specially prepared infant cereals now contain substantial amounts of added vitamin D, and many babies receive vitamin supplements in addition, and may be receiving so much as to be harmful. The author therefore organized a survey in West Ham, London, of 299 babies aged 3 months; 32% were completely or partially breast-fed, and of the remainder most were fed on national dried milk.

The result showed that 23% received less than 600 IU vitamin D daily, 25% received 600–1,000 IU, 51% received 1,000–2,000 IU, and 1% over that amount. Except for the breast-fed babies, all were receiving unnecessarily large amounts of vitamin D. The survey showed, however, that almost all were receiving too little vitamin C, and the author emphasizes the fact that dried milk does not contain vitamin C.

Charles Wilcocks

RAMSAY, Dorothy H. E. & HARVEY, C. C. **Marking-Ink Poisoning. An Outbreak of Methaemoglobin Cyanosis in Newborn Babies.** *Lancet.* 1959, May 2, 910–12. [11 refs.]

Although the danger to new born babies of certain types of marking ink used on napkins has been known for over 70 years, mishaps due to this ink continue to be reported from time to time [this *Bulletin*, 1953, v. 28, 1008; 1955, v. 34, 93].

This paper contains a good account of an outbreak of cyanosis in a maternity home in which 6 new born babies were affected. In 5 of these babies the cyanosis disappeared within 24 hours. The sixth infant became severely ill and his clinical state is described. He was treated by ascorbic acid (200 mgm. by mouth) and 5·0 mgm. of methylene blue intravenously. Almost immediately after the injection he began to improve and within 15 minutes his skin had an entirely normal colour.

At this maternity home all napkins had for several years been marked by a sewing machine but owing to a breakdown in the return of laundry 72 new napkins from stock were marked with old marking-ink and were made available for use without being laundered first.

"Renewed publicity needs to be given every year to the importance of fixing marking-ink before garments are used, and this subject might be given prominence in all refresher courses for midwives." *M. E. Delafield*

Care of Old Persons and the Chronically Ill

EDWARDS, Felicity, MCKEOWN, T. & WHITFIELD, A. G. W. **Incidence of Disease and Disability in Elderly Men.** *Brit. J. Preventive and Social Med.* 1959, Apr., v. 13, No. 2, 51–8, 2 figs.

"Our statistical knowledge of the implications of ageing may be summed up by the statement that it is possible to assess the chances of living to be old, but not whether it is worth doing so." In a previous paper [this *Bulletin*, 1958, v. 33, 548] the incidence of disease and disability and of fitness for employment was examined in a group of representative men aged 60–69 and the enquiry is extended in the present paper to men over 70 but with a somewhat different treatment of the data. These data were obtained by the same 11 Birmingham general practitioners who agreed to attempt the assessment of all men on their lists aged 70 years and over. The information collected concerned: (a) medical data, (b) type and frequency of care required, (c) employment and fitness for employment and (d) personal data which included observations on sleep, drink, food and smoking habits. Men were also asked to state their 3 chief sources of pleasure and their 3 chief complaints. The number of men of 70 or over on the lists was 838 but of these only 691 were available for examination.

The data are set out in tables by age distribution and social class and by frequency of the 6 disease groups—bronchitis, hypertension, coronary disease, arthritis, hernia and peptic ulcer, and the extent to which these diseases caused disability. Other tables give information on habits, pleasures and complaints.

Among the findings were: (1) of the 6 disease groups, bronchitis, coronary disease and arthritis were associated with a high incidence of disability, (2) only bronchitis had a marked association with social class, (3) 64·7% of the men would be restricted from full employment by disability, 13·2% would not be so restricted and 22·1% were not disabled and (4) the chief pleasure was gardening (22·6%) and the chief complaint was "poor health" (35·7%). The proportion of men who complained of poor sleep or poor appetite was very small.

M. E. Delafield

EDWARDS, Felicity, MCKEOWN, T. & WHITFIELD, A. G. W. **Contributions and Demands of Elderly Men.** *Brit. J. Preventive and Social Med.* 1959, Apr., v. 13, No. 2, 59–66, 2 figs.

The data on which this paper is based were obtained from the 691 men aged 70 and over by the 11 Birmingham practitioners some of whose observations were analysed in another communication [see above]. The care needed by and fitness for employment of these men are now described and the findings set out in a number of tables.

20% of the men were still in full-time employment and of these 31·1% were aged 70–74 and 2·1% were 85 and over. Details are given of 8 men aged 80 or more who were still in full-time employment and an example of these is a man of 82 years, a tool-maker classed as social class III, who had hypertension (260/120 mm.), inguinal hernia and poor sight. The range of the 20% men in full work was 29·2% in Class I to 16·5% in Class V. It is considered that 35·9% of the men were fit enough for their original work and 17·1% fit for work other than their original employment. The class distribution of these men is also given in a table. Over 93% of the men had no need for any form of nursing and 35% required no medical care. *M. E. Delafield*

ROBERTS, G. W. **Boarding-Out of the Elderly.** *Roy. Soc. Promotion Health J.* 1959, May–June, v. 79, No. 3, 246–51. Discussion 251–2.

The boarding-out schemes for the elderly in Plymouth and Exeter have attracted much attention, but that in Flintshire described in this address by the County Medical Officer of Health is less well known, though the success achieved, albeit in a small number of cases, confirms that this type of scheme meets a gap in the provisions for the care of the aged.

This scheme was started in December 1956, and is operated jointly by the County Welfare and County Health Departments. In all, 48 persons were boarded out up to the end of 1958, of whom 22 were then still in foster homes, 4 having died, 4 admitted to hospital, 6 transferred to Welfare Homes and 12 having returned to their own homes or those of relatives. The salient facts are given about 11 of the cases by way of illustration. Points stressed are that not all elderly persons are anxious to be placed with a family, that careful assessment of each case is needed as well as full co-operation with all those who may be concerned, and that it is essential to keep in touch as informally as possible with all those that have been boarded out. Infirmities themselves, however, are not necessarily a bar to such arrangements.

In opening the discussion on the paper, Dr. Wynne GRIFFITH, County Medical Officer of Anglesey, observed that the contribution made was out of all proportion to the number of cases dealt with.

The speaker in answering a number of questions stated that the motive underlying offers to provide foster homes, was he felt, a genuine desire to help the aged. He also suggested that contact with others with outside interests was an important factor in maintaining physical and mental health. *C. O. S. Blyth Brooke*

Vital Statistics and Epidemiology

GENERAL REGISTER OFFICE. **Studies on Medical and Population Subjects No. 15. Social and Biological Factors in Infant Mortality** [HEADY, J. A. & HEASMAN, M. A.]. pp. viii + 195, 7 diagrams. 1959. London: H.M. Stationery Office. [20s.]

Much of the basic statistical data derived from an enquiry into the deaths in infancy of children born in 1949 and 1950 are here assembled in a convenient form in order "to make available this information for the benefit of those who may wish to make further study of it". The enquiry was carried out jointly by the Social Medicine Research Unit of the Medical Research Council and by the General Register Office.

In the introduction it is stated that the enquiry was concerned with about 1½ million births which occurred in England and Wales in the 2 years. Of these 33,000 were stillbirths and 44,000 deaths occurred in the first year of life. The data were analysed "to study the action and interaction of certain social and biological factors on the infant mortality and stillbirth rates". The main results of the enquiry have been published in a number of papers under the title "Social and Biological Factors in Infant Mortality" (*vide* list of these in Appendix I [see, for example, this *Bulletin*, 1955, v. 30, 392, 477]) and further papers in the series will appear in due course. Methods used in the enquiry are described and there is a list of definitions.

The valuable and elaborate statistical data and their

detailed analysis are clearly set out in about 160 pages of tables and there are also 7 diagrams. In addition to the appendix which records the papers already published there are 3 others which give (1) the constitution of the standard regions of England and Wales, (2) the constitution of the conurbations and (3) a list of the analyses, considerably more detailed than those given in the tables or in published papers, which can be consulted at the General Register Office or at the Social Medicine Research Unit of the Medical Research Council. Photostat copies of these can also be obtained on payment of the cost of photography (Appendix II).

M. E. Delafield

ANTOINE, M. & CHOLLET, P. A propos de la mortalité infantile dans une oasis du Sahara constantinois (El Oued). [**Infant Mortality in a Sahara Oasis in the Constantine Area (El Oued)**] *Arch. Inst. Pasteur d'Algérie.* 1959, Mar., v. 37, No. 1, 61–72.

The usual indices for comparative purposes cannot be found in the area studied but there is evidence that mortality is very high among children. Of the 904 deaths in 1955 72·5% were in subjects under the age of 15 and of the 1,082 deaths in 1956 67·7% were in subjects under 15 years of age. For the 2 years combined 368 deaths were of infants under 1 and 520 of infants between 1 and 2 years. The higher mortality in the second year of life differs from the usual trend of the death rates.

The authors interviewed 231 married women with an average age of 31 years. These women had had 1,577 pregnancies of which 1,257 resulted in live births and 320 in abortions. 45% (570) of the children born alive died before reaching the age of 15 and 170 died in the first year of life and 198 between 1 and 2 years.

Infectious diseases are an important cause of death. Measles appears to be very severe; in the outbreak in the autumn of 1955 there were about 700 cases with 50 deaths. Infectious diarrhoea is also a common cause of death. Faulty nutrition, especially after weaning, is an important contributory factor to the high death rate.

The traditional mode of living followed by the married women, and their fatalism, are severe obstacles to the improvement of the conditions of child life. The mother is extremely difficult for the doctor to contact and a sick child, in the majority of cases, arrives at the hospital in the arms of a young girl who is totally ignorant of the infant's condition.

W. J. Martin

DOLL, R. [Edited by.] **Methods of Geographical Pathology.** Report of the Study Group convened by the COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES established under the joint auspices of UNESCO and WHO. 72 pp., 1 fig. [Numerous refs.] 1959. Oxford: Blackwell Scientific Publications Ltd., 24–25, Broad Street. [9s. 6d.]

In the so-called degenerative diseases of middle or later life there is evidence that environmental factors may play an important part. One way of studying these factors is by determining the geographical distribution of each disease throughout the world and relating the differences in incidence to differences in the local environments. The object of this study group was to review techniques used in the past for this purpose and their limitations, to consider more modern methods of approach and to select a small number of diseases particularly suitable for study at the present time. Geographical pathology, as defined in the report, implies comparative studies between different ethnic, national or social groups, whether they live in the same or different countries. It adds to the questions who has *what* and *where* the question *why*? On the other hand it will not be necessarily at all easy to recognize the clue to causation. For example, large international and intranational differences are known to exist in cancer of the stomach but no satisfactory hypothesis about the cause of the disease has so far come from these observations. Correlations in space may be as misleading as correlations in time and proof of causation will require detailed evidence of the conjunction of cause and effect in the individual as well as in the community.

Taking the classical methods of study the report reviews in detail the value and weaknesses of mortality rates by cause of death, autopsy data, hospital records and morbidity statistics. The value of all such material can be greatly enhanced by close attention to the method of collection and presentation, *e.g.* by such factors as age and sex. In the survey of morbidity the aim should be to measure the incidence of a disease, *i.e.* the number of new cases occurring in a specified time in a specified population. The point prevalence, *i.e.* the number of cases existing at a given time, is less useful since it is influenced not only by incidence but by the duration of the disease and the latter may be affected by environmental factors, *e.g.* treatment. But it must in practice be used frequently. It may be measured by means of surveys of representative samples of a population and one chapter of this report deals lucidly with the problems of identifying and drawing samples, the risks of bias, the identification and measurement of cases and the organization of such a survey. A further chapter discusses registration schemes for such a disease as cancer. Finally the members of the study group agreed on 10 conditions (or groups of conditions) specially suitable for enquiry by the methods of geographical pathology, *viz.* rheumatoid arthritis, blood pressure, atherosclerosis and coronary thrombosis, chronic bronchitis, diabetes mellitus, cancer, congenital malformations, complications of pregnancy and mental disease. Possible methods of approach are briefly discussed. Time for such investigation grows short as uniformity of background increases throughout the world.

[A very useful and clearly written report.]

A. Bradford Hill

KIDD, C. W. & PARK, A. T. **Long-Term Sickness in Northern Ireland.** *Med. Officer.* 1959, June 12, v. 101, No. 24, 327–9.

Long term sickness among the insured population is a serious socio-economic problem in Northern Ireland, the proportion of persons ill continuously for a year

was twice as high as that of Great Britain. The authors have examined the data by age, by 6 clinical diagnoses —respiratory tuberculosis, psychoneuroses and psychoses, arteriosclerotic and degenerative heart disease, hypertensive disease, bronchitis, arthritis and rheumatism— and in 3 groups, men, married women, other women. The proportion per 1,000 of the insured population aged 20 and over who had been continuously incapacitated for at least one year was 26·5 for men, 61·6 for married women and 28·2 for other women. The married women had the largest proportion continuously sick in each age-group, then the other women who had a larger proportion than the males. The long term sickness in each age-group of married women was proportionately 3 to 4 times larger than the males. As would be expected the amount of long term sickness increases with increasing age.

The authors suggest that more sheltered employment is needed for the tuberculosis patient, that more facilities should be available for the treatment of the psychiatric patient and more provision made for rehabilitation, and that in general a sense of urgency and fresh thinking is necessary on many aspects of long term ill health.

[The table of rates should have had the numbers exposed to risk on which the rates were based. These values would allow the reader to correct the 2 errors in the table—at ages 20–64 the tuberculosis rate for married women is given as 8·5 which is larger than any of the age specific rates, and for other women the tuberculosis rate for ages 20–64 is given as 4·4 which is smaller than the rates in the age-groups. The rates for women at all ages tabulated under ages 20–64 may mislead since the age limit for insured women is 60.]

W. J. Martin

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order:—General; Hospital Cross Infection; Diphtheria, Whooping Cough, Streptococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Arthropod-borne Virus Infections; Enteric Fevers.

PUB. HEALTH. 1959, Mar., v. 73, No. 6, 202–36. [32 refs.] **Infectious Diseases.**

World Trends in Infectious Diseases. H. S. GEAR (pp. 202–9).

In some countries the middle of the 20th century has seen the virtual elimination of infectious disease as the significant factor in social life. In a world-wide sense, however, the stage reached is critical rather than terminal. Up to the last 50 to 75 years trends in infectious diseases have been composite. Some diseases, like scarlet fever and diphtheria, showed cyclical incidence and severity not directly correlated with social changes; the sweating sickness of England in the 15th and 16th centuries seems to have flared up once only and then died out. The droplet-borne virus diseases have not even yet yielded spectacularly to the influences of modern civilization and medical science, although the main body of the infectious diseases of history, largely excremental and insect-borne conditions, have greatly decreased.

The fall in the prevalence of infectious disease in its widest sense is largely correlated with the general fall in the mortality of populations and, in the newer countries of Africa, Asia and America, with a marked increase in population—a change which may have important economic, social, and political consequences. Nevertheless, with the massive aid now given by international agencies, such as WHO, this trend is likely to continue. The greatest danger is likely to be a too sudden disturbance of the ecological host-parasite balance, which might permit the re-emergence of traditional scourges, or open the way for new or previously latent diseases, especially of virus type.

Isolation in the Control of Infection. J. GRANT (pp. 210–18).

In Britain there are still great zones of insanitary, overcrowded and inadequate houses, in which isolation of an infectious patient is impossible. Isolation accommodation in hospital is still therefore necessary for serious infectious diseases. Isolation combined with timely vaccination and with disinfection has been conspicuously successful in the control of smallpox, but, considered merely as a preventive of spread of infection, has generally failed in scarlet fever, diphtheria, and the catarrhal infectious diseases such as measles, whooping cough, influenza and the common cold. Enteric fever is highly infectious over a prolonged period and should be nursed in an isolation hospital, and where the illness is severe enough to warrant hospital treatment this should apply also to salmonellosis and dysentery. Modern drug therapy commonly renders tuberculous patients non-infective, but an intensive search should be made for all infectious patients, who should be segregated until rendered non-infective. Poliomyelitis and meningococcal disease may be highly infective conditions in the early acute stage, and should not be nursed in open wards in general or children's hospitals. Patients with drug-resistant

staphylococcal infection in surgical, maternity, and other hospitals, should be treated in isolation, each in a separate cubicle.

Intestinal Infections. A. B. CHRISTIE (pp. 219–22).

Beds must be provided in isolation hospitals for patients with enteric fever, for those acutely ill with salmonellosis or dysentery or with staphylococcal enteritis, and for children and adults infected in other institutions, however mild their illness. But admission of patients on bacteriological rather than clinical grounds should not be sought unless as part of a well considered epidemiological plan; routine admission of carriers is impracticable and most attempts at it unrewarding. A patient with a mild intestinal infection can often be treated at home, but usually the other children in the house will be infected and require treatment as well, and the drug used for treatment should always be one to which the local strain of the causal organism is known to be sensitive.

Pyogenic Meningitis. G. D. W. MCKENDRICK (pp. 223–8).

A patient with this disease should be nursed in isolation and in hospital, where a speedy and certain diagnosis can be made and rational drug and other treatment applied. The following routines are suggested for treatment, according to the organism found in the spinal fluid or blood:

Meningococcus	
(1) Sulphadimidine	0·3 gm. per kgm. per 24 hours (in divided doses, every 4 hours—for 2–3 days).
or	
Sulphadiazine	0·2 gm. per kgm. per 24 hours to total of 7 days. Give sodium salt i.m. till vomiting ceases.
+ (2) Penicillin	500,000 units i.m. every 6 hours for 5 days in toxic cases and those with any clinical evidence of septicaemia.
Haemophilus influenzae and *Escherichia coli*	
(1) Sulphonamide	as for meningococcus.
+ (2) Chloramphenicol	200 mgm. per kgm. per day (in divided doses, every 6 hours) (maximum dose 4 gm. per day) for 2–3 days. 100 mgm. per kgm. to total of 10–14 days.
or	
Streptomycin	40 mgm. per kgm. per day (in divided doses every 12 hours) for 14 days.
+ Streptomycin	25–100 mgm. i.t. daily for 7 days.
Pneumococcus and Streptococcus	
(1) Penicillin	10,000 units i.t. under 2 years } Daily for 20,000 units i.t. over 2 years } 7–10 days.
+ (2) Penicillin	500,000 units every 6 hours i.m. for 14 days.
+ (3) Sulphonamide	as for meningococcus.
Staphylococcus	
Penicillin-sensitive	as for pneumococcus. i.t. penicillin may be necessary every 12 hours for first 2 days.
Penicillin-resistant	according to sensitivity.
Ps. Pyocyanea	
(1) Polymyxin	2·5 mgm. per kgm. per 24 hours (in divided doses every 8 hours) for 4 days.
+ (2) Polymyxin	2·5 mgm. i.t. daily for 4 days.
+ (3) Streptomycin	40 mgm. per kgm. per day i.m. for 7–14 days.
Listeria monocytogenes	
(1) Sulphadiazine	as for meningococcus.
+ (2) Chloramphenicol	as for *H. influenzae*.
Unknown	
(1) Sulphonamide }	as for meningococcus.
+ (2) Penicillin }	
+ (3) Chloramphenicol	as for *H. influenzae*.

i.m. = intramuscular i.t. = intrathecal

Infancy is the worst age for any type of meningitis. Staphylococcal and streptococcal meningitis are more serious than the commoner forms. The case fatality rate of meningococcal meningitis treated in hospitals for infectious diseases in large representative series during the last 20 years has been 0 to 7%. In pneumococcal meningitis, the prognosis is related to the intrathecal use of penicillin for an adequate length of time; a representative case fatality is 15%. *H. influenzae* meningitis should have a recovery rate of 95%. [No infant over 3 months of age with meningococcal meningitis should have less than 3 gm. sulphonamide daily for the first 3 days—then it should be reduced. Soluthiazole is a far better soluble sulphonamide than any sodium salt—it is neutral and bland, not highly alkaline and irritating.]

Lymphocytic Meningitis. W. M. JAMIESON (pp. 229–36).

This term now includes: (1) tuberculous meningitis; (2) virus meningitis due to (a) enteroviruses (poliomyelitis, Coxsackie, ECHO), (b) lymphocytic choriomeningitis (due to LCM virus), (c) mumps, (d) glandular fever, (e) herpes zoster, (f) herpes simplex; (3) spirochaetal meningitis due to (a) syphilis, (b) leptospirosis. Many cases are, however, of unknown aetiology.

Except for tuberculous and syphilitic meningitis, the disease is mainly benign, and there is no specific treatment. Cerebral abscess is sometimes a cause of lymphocytic meningitis, when it is situated near the meninges.

H. Stanley Banks

GIORN. DI MALATTIE INFETTIVE, E PARASSIT. 1958, Sept., v. 10, No. 9, 659–862, numerous figs. [Numerous refs.] Società Italiana per lo Studio delle Malattie Infettive e Parassitarie. IX Congresso Nazionale, Taormina, 5–8 dicembre 1957. **[Ninth National Congress of the Italian Society for the Study of Infective and Parasitic Diseases, Taormina, December 1957]**

The record of this meeting includes the text of 93 papers of varying length and dealing with a wide variety of subjects, including antibiotics, bacterial, viral, fungal and protozoal infections. Most of the authors of the papers are Italian, and as usual this publication gives an impression of Italian work and opinion on the subjects with which it deals. But it is not practicable to say more than that the papers should be read in full.

Charles Wilcocks

GIORN. DI MALATTIE INFETTIVE E PARASSIT. 1958, Nov., v. 10, No. 11, 944–1256, numerous figs. [Numerous refs.] Società Italiana per lo Studio delle Malattie Infettive e Parassitarie. X Congresso Nazionale, Bologna 7–9 dicembre 1958. **[Tenth National Congress of the Italian Society for the Study of Infective and Parasitic Diseases, Bologna, December 1958]**

This issue of the *Giornale* comprises 6 long papers, each of which is a comprehensive essay on its subject, summing up modern work. The first, by A. ZIRONI (pp. 944–78) deals with the problems of adaptability of

the body to bacterial and other antigens, and covers the subject of allergy as well as immunity.

This is followed by 2 papers on the virological aspects of tumours and malignant diseases of the blood, by F. MAGRASSI (pp. 981–1016) and V. CILLI (pp. 1017–40) who writes on the Shope fibroma and the Sanarelli myxoma.

The last 3 papers relate to infective enteritis in adults and children, R. DE BLASI and G. SANTOPADRE (pp. 1043–104) writing on the aetiology, epidemiology and prophylaxis of bacterial, fungal, viral and protozoal infections, A. GENTILI, W. TANGHERONI and L. POLI (pp. 1105–197) on infective enteritis of infants and L. CANNAVO (pp. 1199–256) on infective enteritis in adults.

Most of the papers include long lists of references and should prove most useful to readers of the Italian language who wish to follow recent work on these subjects. *Charles Wilcocks*

SCRIMSHAW, N. S., TAYLOR, C. E. & GORDON, J. E. **Interactions of Nutrition and Infection.** *Amer. J. Med. Sci.* 1959, Mar., v. 237, No. 3, 367–403. [378 refs.]

This paper cannot be summarized because it is itself a summary of the literature on subjects within the scope of its title. Numerous field and laboratory observations have indicated an association between nutrition and infection, malnutrition usually resulting in increased susceptibility to infection and a good nutritional state being associated with resistance to infection. The literature on this subject is very thoroughly explored, no less than 378 references being listed and summarized in a few words. The authors use the term "antagonism" to describe the situation where factors decrease the frequency or severity of infection and "synergism" where factors increase its frequency or severity. A general conclusion is drawn that when the main action of nutritional deficiency is on the host synergism results, and when the main action is on the infectious agent antagonism results.

The subject is discussed in a number of sections. The first, on patterns of interaction, includes lengthy tables giving the findings of various workers in regard to the effect of nutritional deficiencies of various kinds on infection due to different agents (bacterial, viral, rickettsial, helminthic and protozoal) in different hosts. Then follow sections on mechanisms of antagonism, the influence of infection on nutritional status, lines along which research would be useful, some common misconceptions, and working generalizations. It is concluded that in human populations interaction between nutrition and infection is probably more important than laboratory investigations would indicate; that synergism is the dominant interaction; that the type of synergism in which infections contribute to malnutrition needs more attention; that the addition of nutrients to an adequate diet does not affect infections; that the antagonism demonstrated between nutritional deficiency and viral and protozoal infections has no recognized practical usefulness; that antagonism appears only where organisms are dependent on the enzyme systems of host cells.

This paper is of interest on account of the broad conclusions drawn from a large amount of research and has great value as a record of the literature on the subject. *T. H. Davey*

WILLIAMS, J. R. B., TALBOT, E. C. S. & MAUGHAN, Elizabeth. **Hospital Outbreak of Cross-Infection due to Staphylococcus Pyogenes Phage Type 80.** *Brit. Med. J.* 1959, May 30, 1374–8, 1 graph. [11 refs.]

This paper describes an epidemic of infection due to staphylococci of phage type 80 in a general hospital; as all the lesion strains proved to be tetracycline-resistant, tetracycline (10 mgm. per ml.) was incorporated in the culture plates used to seek carriers and environmental contamination.

During the year 1957 to June 1958, the male surgical ward recorded 45 cases of sepsis due to resistant staphylococci, of which 30 were type 80; the average number of admissions per month was 72. Lower rates were observed in other wards. Of 267 lesions (175 type 80), 70 (48) were wound infections, 23 (10) urinary tract, 35 (16) respiratory tract, and 135 (101) skin lesions. From the distribution of cases, it seemed that cross-infection in the wards was responsible for most of the wound infections. 10 patient with type 80 infection were recorded in general practices in the locality.

Attempts were made to control the outbreak, first, by closing and cleaning each ward in turn and by attention to carriers; hexachlorophene soap and chlorhexidine hand cream were used by the staff, and any nasal carriers among patients or staff were treated with neomycin ointment applied to the anterior nares. After closure of a ward only staff known not to be nasal carriers of tetracycline-resistant strains were allowed into it and any patient developing a lesion due to a similar strain was removed to an isolation ward.

The use of neomycin ointment intranasally led to a rapid reduction in the proportion of nurses carrying tetracycline-resistant strains. 17 skin carriers studied in detail were mostly cleared of infection in 1 week and all but 1 were clear in 4 weeks. The 1 was a persistent carrier for 3 months. The presence of a septic lesion was almost always associated with skin carriage.

The nasal neomycin did not reduce nasal carriage among patients quite so effectively and 21 patients were persistent carriers resisting all treatment. An attempt to prevent the acquisition of the staphylococci in the nose, by giving local neomycin to all patients from the day of admission, did not appear to have the desired effect.

In sum, therefore, attempts to stop the epidemic of type 80 infections were not successful. The authors think that this was probably due to their inability to isolate all the carriers of the epidemic type as well as the patients with septic lesions. *R. E. O. Williams*

RALSTON, Mary & COWLING, D. C. **A Survey of Wound Infection at the Royal Melbourne Hospital.** *Med. J. Australia.* 1959, Mar. 28, v. 1, No. 13, 424–6.

Of 357 clean surgical operation wounds, 21 (5·9%) developed post-operative sepsis, 12 with moderate or

much purulent discharge. 91 other operation wounds were clean but were considered, from the nature of the operation, potentially infected; 15 (16·5%) developed sepsis, in 7 cases serious. Of the first group 15, and of the second 5, yielded *Staphylococcus aureus* on culture.
R. E. O. Williams

MIDDLETON, R. W. D. **Wound Infections.** *Med. J. Australia.* 1959, Mar. 28, v. 1, No. 13, 426–8.

As illustration to a general discussion on the problems of wound sepsis the author quotes the results of recording all post-operative infections in an orthopaedic unit at the Royal North Shore Hospital, Sydney for 6 months in 1958. Of 118 clean operations, 8 (6·5%) developed sepsis, 1 seriously. *R. E. O. Williams*

FORSGREN, U. & VARENIUS, P. Nosocomial staphylococcinfektion på en neurokirurgisk avdelning. Bakteriologiska och preventiva aspekter. [**Nosocomial Staphylococcal Infections in a Neurosurgical Ward**] *Opuscula Med.* Stockholm. 1958, Oct., v. 3, No. 8, 293–300. [19 refs.] English summary.

In an outbreak of staphylococcal infection involving 6 patients in a neurosurgical ward in a Stockholm hospital which has already been described [this *Bulletin*, 1959, v. 34, 726], an investigation of the staff showed that 19 of 39 persons were carrying *Staphylococcus aureus* in the nasopharynx, and the organism could also be recovered from the floor and air of the ward. 6 of the strains isolated from the carriers showed a spectrum of antibiotic resistance identical with that of the strains isolated from the affected patients. The phage-type combinations most frequently encountered were I 80/KS 6, II 3A and III 47/73/75/77/1034. Measures to combat the spread of infection were introduced, such as improvements in sterilization and disinfection and limitations in the use of antibiotics. In a repeated examination carried out after 2 months no new infections had occurred among the patients; 28 of the staff were found to be carriers of *Staph. aureus*, but none of the strains isolated had the same phage-type combination as the strains isolated from the patients. *D. J. Bauer*

RANFT-HÄUSSLER, A. & PÖHN, H. P. Beobachtungen über die Ausbreitung von Staphylokokken-Mastitiden in einer geburtshilflichen Klinik. Ein Beitrag zur Frage des Staphylokokken-"Hospitalismus". [**Observations on the Spread of Staphylococcal Mastitis in an Obstetric Hospital**] *Deut. med. Woch.* 1959, Apr. 24, v. 84, No. 17, 817–20, 851–2, 3 figs. [Numerous refs.]

Between January and March 1957, 31 patients in an obstetric hospital developed mastitis from which *Staphylococcus aureus* was isolated; in 28 the strain belonged to the phage type "80/7/73 . . .". Investigations of 42 women and their infants in the hospital in March revealed that 13 of them harboured the epidemic type, as did 8 of 25 staff. 22 of the women and infants harboured another type, "7/77/42D . . .". Both these types were present in a small proportion of samples of air and fomites. The 2 hospital types were not commonly found in mothers or infants before the 4th day of the puerperium. [Nowhere are the figures for mothers and infants given separately.]

There is extensive discussion of these observations in the light of reports published elsewhere, and in particular of the suggestion that different phage types of staphylococci may vary in virulence. *R. E. O. Williams*

COLES, R. B. **Observations on a 12-Months' Survey of Staphylococcal Sepsis in Maternity Home.** *Pub. Health.* 1959, May, v. 73, No. 8, 285–91, 1 fig.

A 72-bed maternity unit having about 150 deliveries per month, experienced between March 1956 and February 1957 an incidence of sepsis [apparently mostly among the babies] of 5–15 cases per month. Disinfection of blankets, the use of hexachlorophene-containing soap and chlorhexidine hand cream, nasal application of neomycin-bacitracin cream by the nurses, oiling of floors, and the abandonment of face masks had no detectable effect on the sepsis rate. Cases of sepsis were transferred to an isolation ward whenever possible.
R. E. O. Williams

KLEIN, J. O. & ROGERS, Evelyn F. H. **Use of a Nasal Antibiotic Cream During a Nursery Outbreak of Staphylococcal Disease.** *New England J. of Med.* 1959, May 14, v. 260, No. 20, 1012–15, 1 fig.

Skin lesions were noted by public health nurses to be occurring in a rather large proportion of infants discharged from a maternity hospital in New York; 59 of 97 discharged in a 2-month period were examined and 19 (32%) found to have significant lesions. Staphylococci of type 80/81 were recovered from several of the lesions. Only 4 of 30 members of the staff harboured this type.

As the attack rate, determined by home visiting, continued high, all the staff and infants in the hospital were, for one week in March, treated with a neomycin-gramicidin ointment to the anterior nares 4 times daily. During the same period a new nursery was "set up" and all techniques were reviewed. In the 4 months April to July no case of sepsis was recorded.

[It is not stated whether bacteriological studies were made to discover whether there was any change in the dominant staphylococci in the hospital.]
R. E. O. Williams

UNITED STATES NATIONAL LIBRARY OF MEDICINE. Reference Division. **Staphylococcal Infection. A Bibliography, covering Literature of 1952 through May 1958.** 43 pp. 1958, June. Wash., D.C.: U.S. Dept. Health, Education & Welfare, Pub. Health Service.

NORGAARD, A. **Diphtheria Vaccination. The Danish National Morbidity Survey of 1950.** Communication No. 22. *Danish Med. Bull.* 1959, May, v. 6, No. 3, 94–6, 1 graph.

During the morbidity survey of 1950 opportunity was taken to find out how many adults had been inoculated

against diphtheria. For the country as a whole the percentages (to the nearest whole number) were 93 at 15–19 years of age, 87 at 20–29, 64 at 30–39, 47 at 40–49, 30 at 50–59, 18 at 60–69 and 10 at ages above 70. At ages above 30 the proportion was considerably higher in the capital than in the provincial towns and slightly higher in the provincial towns than in the rural districts. At ages above 40 more women than men had been inoculated. *A. Bradford Hill*

JANSSON, E. & KLEMOLA, E. **Effect of Penicillin Therapy on Occurrence of Second Attacks in Scarlet Fever.** *Brit. Med. J.* 1959, May 30, 1382–4, 2 figs.

Observations on 7,837 patients with scarlet fever treated with penicillin in the Aurora Hospital, Helsinki, over the 6½ years 1947–1956 showed that early secondary attacks (within 3 months of the primary infection—or "relapses" as we would call most of them) occurred in 1·4%, and late second attacks in 5%—a fairly high figure. The interval between the first and second attacks was in most cases less than 2 years, and the second attacks occurred most commonly in children under 7 years, and were uncommon over 15 years of age. The likelihood of a second attack was increased when penicillin treatment was started before the second day of disease—thus probably interfering with the development of full immunity. A different possible cause of second attacks exists, however, when the new invading streptococcus produces a different kind of erythrogenic toxin from that operating in the primary attack.

These observations provide no grounds for omitting or postponing penicillin therapy in scarlet fever.

H. Stanley Banks

TERRAGNA, A. L'importanza epidemico-profilattica della via congiuntivale nel morbillo. [**The Epidemiological and Prophylactic Importance of the Conjunctival Route in Measles**] *Giorn. di Malattie Infettive e Parassit.* 1959, Apr., v. 11, No. 4, 293–7. [13 refs.]

The author refers to DE TONI's description of subepithelial nodules in the outer third of the lower tarsal conjunctiva which appear as the earliest manifestation of measles and to PAPP's theory [this *Bulletin*, 1959, v. 34, 108] that the conjunctiva is the mode of entry of the measles virus. To test the epidemiological importance of the theory he exposed groups of children to patients suffering from measles and attempted to prevent infection by instilling a drop of convalescent serum into the conjunctivae of the exposed children. 12 children were exposed to measles, isolated after the first day, and given 1 drop of convalescent serum into the conjunctivae each day for 7 days: only 1 child developed measles. 6 children were given the drops 2 to 3 days after infection and then repeatedly: all developed measles after a prolonged incubation period. 6 children were given drops once only 4 days after exposure: all developed measles after the normal incubation period. 9 children were given the drops repeatedly from the first day of exposure but were not isolated from infection: these all developed measles, 6 of them after a long incubation period.

The author feels that, though his numbers are low, and do not confirm Papp's assertion that the conjunctiva is the only route of entry for the measles virus, they do add a little to the better understanding of the epidemiology of measles and give some hope of improvement in the prophylaxis of the disease.

[See also PAPP, above, p. 969.] *A. B. Christie*

KARELITZ, S. & ISENBERG, H. D., with the assistance of S. B. GITTELSON & M. STILLERMAN. **The Antibiotic Prophylaxis of Bacterial Complications of Measles.** *J. Pediatrics.* St. Louis. 1959, Jan., v. 54, No. 1, 1–10, 2 figs. [13 refs.]

Differences of opinion still exist as to the use of antibiotics in the prophylaxis of the complications of measles, and this article is a real contribution to the problem. It shows that the divergent opinions expressed are probably due to observations based on non-comparable groups, especially in respect of age, socio-economic environment, and the microbiological milieu in which the studies were conducted.

Antibiotics (most commonly penicillin or erythromycin) were given prophylactically to 88 children with measles at home—these were mostly between 4 and 10 years of age, and of middle social grade—and also to 24 children with measles in hospital who were mostly below 3 years of age and of lower socio-economic grade. None developed complications of the usual type commonly referred to as "superinfections". Of the 88 children at home 14 developed ordinary complications mostly mild otitis media, within 1 to 11 days after the drugs were discontinued. None of the 24 children in hospital developed complications while there. In general these groups of children who had antibiotics prophylactically at home or in hospital fared better than those who did not have them.

It is concluded that certain groups should be particularly selected for antibiotic prophylaxis of complications during an attack of measles: (a) children under 3 years of age, (b) children or adults who are ill with pulmonary infections, such as chronic bronchitis, tuberculosis, or cystic disease, and those with otitis media, sinusitis, rheumatic fever, other serious cardiorespiratory illness, and (c) older individuals and pregnant women with measles. Any of these categories who have had gamma globulin prophylaxis during the early incubation period could, however, be excluded, since in such cases measles is likely to be modified, if it occurs at all.

H. Stanley Banks

MONGAN, E. S. **The Treatment of Mumps Orchitis with Prednisone.** *Amer. J. Med. Sci.* 1959, June, v. 237, No. 6, 749–53.

"A double-blind forward-looking study comparing the results of therapy in patients with mumps orchitis treated either symptomatically, or with a placebo, or with prednisone; revealed no differences in the course of the disease in the three groups."

REV. D'IMMUNOLOGIE. 1958, July–Sept., v. 22, No. 4, 235–460, numerous figs. [Numerous refs.] Séminaire sur la Coqueluche, organisé par Le Centre International de l'Enfance, Paris, 16–17–18 décembre 1957 [DEBRÉ, R., President]. **[Seminar on Whooping Cough by the International Children's Centre, Paris]**

This volume of the journal gives full reports of the lectures and discussions given at a conference on the problems of whooping-cough held in December 1958 at the International Children's Centre in Paris.

The conference had four main sections: 1. Bacterial diagnosis of whooping-cough; 2. Whooping-cough vaccines: production and study methods; 3. The application of whooping-cough vaccines; 4. Nursing of infants with whooping-cough.

1. *Bacteriological diagnosis of whooping-cough*

F. HERZOG and M. GAIFFE (pp. 235–258) presented their studies on the bacteriological diagnosis of whooping-cough from mucus aspirated from the naso-pharyngeal area. Details of their new aspirating technique are given and a new medium incorporating X-irradiated blood is described which, because of a rapid growth of the organisms, allowed an earlier diagnosis of the disease to be made. Much of the discussion of the paper centred around the effect of irradiation of the blood in the medium.

2. *Whooping-cough vaccines*

Three aspects were considered:—

(a) *Preparation of the vaccines*: J. CHEVÉ (pp. 259–265) emphasized the importance of using several phase I strains for the preparation of each vaccine. The media used for growth of the organisms were reviewed and it was reported that merthiolate had replaced phenol as the bactericidal agent, although some manufacturers used formalin. Methods of control of antigenic activity were outlined and it was pointed out that both plain and alum-containing vaccines are available.

The alternatives to these methods existing in several laboratories in many countries were enumerated in the discussion which followed.

(b) *Methods of studying the vaccines*: E. K. ANDERSEN (pp. 266–276) outlined two biological tests for the determination of potency of the vaccines. In both tests mice are immunized with a single dose of vaccine and subsequently challenged with virulent organisms. In one an intracerebral challenge is used while in the other the challenge organisms are given intranasally. The effect on the results of varying the challenge dose and time of challenge are discussed.

In the discussion, V. KRATOCHVILOVA reported that the results obtained by K. RASKA and J. JELINEK differed from those of E. K. Andersen [this *Bulletin*, 1958, v. 33, 179], who confirmed the work of EVANS and PERKINS [*ibid.*, 1956, v. 31, 83].

D. G. EVANS (pp. 277–284) reported the results obtained by Evans and Perkins using an agglutinin production test in which the agglutinin titres were determined in sera from mice taken after giving 2 doses of vaccine. The results obtained with Pillemer's antigen (SPA) [*ibid.*, 1955, v. 30, 548] were also mentioned.

In the discussion N. DATTA showed that there was good correlation between the ability of several vaccines to protect infants against whooping-cough and to produce agglutinins in children as well as in mice. E. K. ANDERSEN reported that G. ELDERING found that mice give high agglutinin titres to Pillemer's antigen when Pillemer's strain was used as antigen in the agglutinin test.

F. M. LÉVY (pp. 285–292) gave his results on agglutinin titres in vaccinated subjects and reviewed the published results of many workers with both single and combined vaccines, some of which contained a mineral carrier. Lévy concluded that for whole bacterial vaccines the measurement of agglutinin response in children was a convenient measure of antigenic activity.

J. UNGAR (pp. 293–307) presented the results obtained in children to pertussis vaccine and pertussis-diphtheria vaccine, both plain and adsorbed. The responses after 3 doses were very much better than those after 2 doses and adsorbed vaccines also gave higher antibody levels.

(c) *The activity of different vaccines*: Margaret PITTMAN (pp. 308–322) showed how whooping-cough is a far more lethal disease than any other infection, including poliomyelitis. A good correlation was shown between the ability of vaccines to protect mice against intracerebral infection with pertussis and protection of children against whooping-cough. The number of organisms injected is not a reliable criterion of the protective power of the vaccine. It was shown that the vaccines were stable for at least 3 years.

M. PONTECORVO (pp. 323–336) dealt with some details of the production of combined vaccines and presented data from both children and animals showing the superior immunizing efficiency of pertussis vaccine containing an adjuvant compared with those of plain vaccines.

3. *The use of whooping-cough vaccines*

R. SOHIER (pp. 337–351) in his lecture on the practice of immunization with plain and combined whooping-cough vaccines, considered the reasons for early vaccination as well as the complications and reactions to the vaccines which have a bearing on the choice of vaccine. In conclusion, the timing of vaccination against whooping-cough in a comprehensive immunization schedule against all infections was discussed.

Jean ZOURBAS (pp. 352–395) presented his immunological and epidemiological studies in more than 15,000 infants vaccinated with plain and combined whooping-cough vaccines which varied their composition of the three antigenic components. The final conclusions were that with either pertussis alone or when combined with diphtheria and tetanus toxoids, the adsorbed vaccines were effective when given in the first few months of life and they were much more effective than the non-adsorbed vaccines. In their trials in nurseries in which contact cases occurred, it was shown that the vaccines were effective in protecting against whooping-cough.

B. VAHLQUIST (pp. 396–418) also presented results of serological and clinical studies on combined vaccines. The antibody levels to each of the antigens after 2 or 3 injections of vaccine are shown and the clinical studies showed the vaccines to be effective in protecting against infections.

W. C. COCKBURN (pp. 419–432) reviewed the data on the incidence of reactions and accidents as a result of whooping-cough immunization, the most serious being

encephalopathy and paralysis of the injected limb due to provoked poliomyelitis.

4. *The treatment of infants and children with whooping-cough*

J. MARIE, G. SÉE and M. GAIFFE (pp. 433–455) reported their observations on the treatment of the disease using the therapeutic substances chloramphenicol, streptomycin, sulphonamides and specific gamma globulins. Using the number and duration of bouts of coughing as well as mortality as an index of effectiveness of treatment, the authors find that gamma globulin therapy in addition to antibiotic injections is essential for reducing the mortality of the disease.

F. T. Perkins

WELSH, J. D., DENNY, W. F. & BIRD, R. M. **The Incidence and Significance of the Leukemoid Reaction in Patients Hospitalized with Pertussis.** *Southern Med. J.* 1959, June, v. 52, No. 6, 643–9. [19 refs.]

"1. The incidence and significance of the leukemoid reaction in pertussis have been compared in two groups of patients. The first group consisted of 47 hospitalized patients seen between 1933 and 1943; the second, 127 patients admitted to the hospital since 1951.

"2. There was found to be no significant difference in the incidence of the leukemoid reaction between the two groups. There was, however, a significant decrease in the incidence of complications and in the mortality rate in the group seen between 1951 and 1956. This improvement was seen almost exclusively in those patients not manifesting a leukemoid reaction.

"3. In those patients whose leukocyte count was in excess of 50,000 per cu. mm., however, complications appeared with similar frequency in both groups and the mortality rate was not significantly different between the two.

"4. It is inferred that the development of a leukemoid reaction in pertussis is of increasing importance in predicting a poor prognosis."

MEDICAL RESEARCH COUNCIL. **Vaccination against Whooping-Cough. The Final Report to the Whooping-Cough Immunization Committee** [BEDSON, S., Chairman] **of the Medical Research Council and to the Medical Officers of Health for Battersea and Wandsworth, Bradford, Liverpool, and Newcastle.** *Brit. Med. J.* 1959, Apr. 18, 994–1000, 1 chart. [12 refs.]

The 3 series of controlled field trials made from 1946 to 1956 in which 19 pertussis vaccines were studied in 36,000 children showed that it was possible by vaccination to produce a high degree of protection against the disease and that vaccines differed in their protective action; the poorest gave an attack rate in home contacts of 87% and the most effective an attack rate of 4%.

At the same time as the field trials were in progress laboratory tests were made in which the vaccines were tested for their ability to protect mice against intracerebral pertussis infection and also for their ability to produce agglutinin in mice. Some of the vaccines were also tested for their ability to produce agglutinin in children. Comparison between the field and laboratory results showed a correlation between protection in children and the three laboratory tests. While the three laboratory tests gave results parallel with those obtained in the field the question of which test gave the most direct measure of factor or factors responsible for inducing immunity in children remained unanswered. An antigenic fraction prepared by the late Professor Louis PILLEMER *et al.* [this *Bulletin*, 1955, v. 30, 548] protected mice against intracerebral pertussis infection but produced a poor agglutinin response, and thus this antigen was included in a final series of field trials to test its ability to protect children against whooping-cough. In the trial about 4,500 children were given Pillemer antigen (SPA) and it was shown that it was able to induce a high degree of immunity in children although it produced an agglutinin response lower than whole bacterial vaccines with equally good protective properties. It was therefore considered that the mouse protection test was the most satisfactory in assessing prophylactic activity of vaccines.

A British Standard Pertussis Vaccine has been prepared from a vaccine giving good protection in the field trials, and by employing this standard in comparative mouse protection tests it will now be possible to ensure that vaccines which are used for immunization against whooping cough will produce substantial protection against the disease. *F. T. Perkins*

JOÓ, I., PUSZTAI, S. & JUHÁSZ, V. Immunantworten auf verschiedenartig angewandte Pertussis-, Fluid- und Adsorbat-Impfstoffe. **[Immune Responses to Differently Used Pertussis, Fluid and Adsorbate Vaccines]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, July, v. 118, No. 1, 20–35, 5 figs. [40 refs.]

The English summary appended to the paper is as follows:—

"Immune-responses to differently used pertussis, fluid and adsorbate vaccines.

"During 25 weeks the process of the immune response (agglutinins and mice-protecting antibodies), which was caused by the effect of pertussis, fluid and adsorbate vaccines was tested in groups of rabbits. The results may be summarized in the following manner:

"1. Adsorbate vaccines cause higher immune-responses than fluid vaccines; The difference becomes more clearly obvious in the agglutinin titer.

"2. Prolongation of the interval between vaccinations only slightly increased the immune response concerning the agglutinin titer and the mice-protecting antibodies in the case of fluid vaccines under the prevailing experimental conditions. In the case of adsorbate vaccines, however, the immune-response increases parallelly to the prolongation of the interval in the curves of both antibody titers.

"3. As disclosed by the demonstrated results, the curves of both antibody titers of all vaccinated groups are very similar indeed. The differences within the immune responses of the different groups are generally more clearly evident in the titer of the agglutinins.

"After the problems in question are discussed it is stressed, that the immune response after various vaccinations yields a clear picture only, if examined continuously during a longer period and not only on one or two selected points."

AICKIN, D. R. **A Study of Incidence and Immunisation against Whooping Cough in Dunedin.** *New Zealand Med. J.* 1958, Dec., v. 57, No. 322, 633–7, 1 fig. [12 refs.]

In a study of the incidence of whooping-cough in Dunedin since 1950, it was found that less than 25% of the children under 7 years old had been infected. This was about one-third of the incidence described in 1933. Almost 70% of the children had received some immunization against whooping cough although only about half of them had received a full course of immunization. Non-immunized children showed an incidence of whooping cough 3·5 times greater than immunized children and they were twice as likely to develop whooping cough after close exposure. Children receiving only two injections had an incidence double that of children receiving three injections. It is suggested that a greater emphasis should be placed on the importance of the third dose.

About 20% of children suffered some sort of reaction during or following a course of combined pertussis-diphtheria vaccine. All but 5% were of trivial, local or general nature.

[No note is given of the potency of the vaccines used in New Zealand during the period when the figures were studied.] *F. T. Perkins*

LESNE, E., MARIE, J. & ZOURBAS, J. La vaccination anticoquelucheuse et son importance médico-sociale. [**Vaccination against Whooping Cough and its Medico-Social Importance**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Oct.–Nov., v. 6, No. 7, 793–803.

The authors report their observations after carrying out 50,000 vaccinations against whooping cough in nurseries over a period of 10 years. They find that adsorbed vaccine is much more effective than non-adsorbed. Vaccination against whooping cough should be given in the first 3 months of life and, when combined with diphtheria and tetanus toxoids, in the first 6 months of life.

Because of the seriousness of whooping cough in the very young infant, immunization against this disease should be given as the first prophylactic to all infants.
F. T. Perkins

SOMEYA, S., KANEKO, Y., NAKAHARA, R., KANEKO, A. & KODAMA, M. **Field Studies on the Immunity of Pertussis.** *Bull. Inst. Pub. Health.* Tokyo. 1958, June, v. 7, No. 2, 91–6. [12 refs.]

Intradermal inoculation of pertussis agglutinogen in children gave an induration and erythema of varying degrees. Those children with induration of over 10 mm. after 24 hours or erythema after 48 hours were considered to be immune to whooping cough.

The relationship between the skin reaction and immunity to pertussis was observed in the field for 3 years and shown to have good correlation. Observations on protection rates showed that the Japanese vaccines were potent, and, by using the skin test it was found that an alum-precipitated vaccine gave a higher positive conversion rate than plain vaccine. *F. T. Perkins*

CROCKER, A. M. & MIDDELKAMP, J. N. **Varicella Gangrenosa.** *J. Pediatrics.* St. Louis. 1959, Jan., v. 54, No. 1, 104–8, 2 figs. [19 refs.]

A case of gangrene of the extremities in a boy aged 3 years suffering from chickenpox is presented, and the literature of this rare complication is reviewed. The gangrene in this case supervened on areas of ecchymosis or discolouration, which appeared on the 8th day of chickenpox which was also the 4th post-operative day (a herniotomy operation had been performed and thrombosis of the pampiniform plexus found). A blood count at the time of appearance of the ecchymoses showed a gross deficiency of red cells, platelets, and haemoglobin, and a polymorphonuclear leucocytosis. On the next day an area on the mid-foot extending to the toes was seen to be discoloured, and within a few days all these areas of ecchymosis and discolouration became gangrenous, with eventual sloughing of the superficial areas and amputation of the toes.

The authors discuss 4 groups of cases described in the literature: (1) the malnutrition group of the late 19th century; (2) the group due to secondary infection associated with *Corynebacterium diphtheriae, Staphylococcus aureus*, and haemolytic streptococcus; (3) the group associated with a vascular origin, generally characterized by purpura in the first instance; and (4) the group associated with individual susceptibility. [In this fairly wide survey of the literature no mention is made of the fulminating type associated with massive invasion by haemolytic streptococci described by BANKS and MCCARTNEY, this *Bulletin*, 1937, v. 12, 857.]
H. Stanley Banks

STALLONES, R. A. & LENNETTE, E. H., with the technical assistance of Florence W. JENSEN & Vita LESLAU. **Epidemiologic Observations of an Outbreak of Asian-Strain Influenza in a Closed Population.** *Amer. J. Pub. Health.* 1959, May, v. 49, No. 5, 656–67, 3 figs.

The closed community was a mental institution with 2,456 resident patients among whom there were 1,391 clinical cases of influenza with 15 deaths, giving an attack rate of 57% and a case fatality rate of 1·1%. Serological examination showed that the attack rate was higher and it is estimated that between 70–80% of the patients were infected. The outbreak commenced at the end of September and rose rapidly to a maximum on October 8–11 with approximately 200 cases a day and then fell rapidly. About 90% of the attacks occurred in the period October 3–18. The percentage attack rate for males was 62 and for females 51, the difference between the attack rates of the sexes being most marked at ages over 30. Examination by ward of residence

showed that most of the sex difference could be explained by differences between wards. The data have been analysed by type of ward and by the classification of the patients' activity, and generally the more active patients had the higher rates, those attending school had the highest and the bedridden had the lowest attack rates and the habit-trained had a higher attack rate than the patients not habit-trained.

W. J. Martin

BURCH, G. E., WALSH, J. J. & MOGABGAB, W. J. **Asian Influenza—Clinical Picture.** *Arch. Intern. Med.* 1959, May, v. 103, No. 5, 696–707. [31 refs.]

This is a record of the investigation carried out in 76 patients suffering from influenza, proved virologically, during August to September 1957 in the New Orleans area. Clinical symptoms and signs are analysed and there are details of X-ray findings, electrocardiography, spatial vectorcardiography, haematology, serology, hepatic and renal function, serum enzymes estimations, fluid and electrolyte studies, bacteriology, cerebrospinal fluid examinations, analyses of temperature, pulse, and blood-pressure findings and a survey of associated clinical states. The outbreak appeared to be a mild one.

A. B. Christie

SKANSE, B. & MIÖRNER, G. **Asian Influenza with Adrenocortical Insufficiency.** *Lancet.* 1959, May 30, 1121–2.

This short article is of interest in drawing attention to the effect of untreated adrenocortical insufficiency on the prognosis of Asian influenza. In Malmö, Sweden, there were 9 deaths in 1957 among the 220 patients admitted to hospital with Asian influenza. At least 4, and probably 5, of the deaths were in patients with untreated or under-treated adrenocortical insufficiency; 2 of these, aged 29, and 65, had untreated Addison's disease, 1 aged 66 had untreated panhypopituitarism, and 1 aged 18 had a gangliocytoma with adrenocortical atrophy. Of these 4 patients 3 showed no response to intense replacement therapy, and the 4th was dead on admission. The 5th patient, aged 31, died from perforated gastric ulcer and influenza with adrenal failure, which was secondary to long-continued cortisone treatment of rheumatoid arthritis.

Further points made by the authors are (1) that of 5 patients in the hospital on adequate substitute treatment of adrenocortical insufficiency, influenza was mild in 4 and severe in only 1, and (2) that of 12 patients with adrenocortical insufficiency who were vaccinated against influenza in the hospital, only 2 developed influenza, which was fairly mild in both. It is concluded that resistance to influenza is severely reduced in patients with untreated adrenocortical insufficiency, but not in those on adequate replacement therapy.

H. Stanley Banks

BOURNE, G. & WEDGWOOD, J. **Heart-Disease and Influenza.** *Lancet.* 1959, June 13, 1226–8, 2 figs.

The exact causal relationship between heart disease and influenza has never been established. The literature suggests: (1) that rapidly fatal cases of acute myocardial involvement occur in influenza, (2) that in most cases of less severe influenza there is no strong evidence of cardiac involvement, and (3) that influenza appears to precipitate cardiac abnormalities in patients previously suffering from heart disease.

14 cases seen during the 1957 epidemic of Asian influenza are described. In 6 of these influenza would seem to have caused definite cardiac complications, and in the other 8 to have brought them to the surface; the 8 cases of auricular fibrillation, and the 4 cases of coronary ischaemia were equally divided between these two groups. The age of the patients 47–70 (average 57) suggests that in all of them the heart may not have been perfectly normal.

Influenza appears to have a definite though temporary effect upon the myocardium, perhaps by causing cloudy swelling or some lesser change.

H. Stanley Banks

FORBES, J. A. **Severe Effects of Influenza Virus Infection.** *Med. J. Australia.* 1958, July, 19, v. 2, No. 3, 75–9, 2 figs.

This is a report of the clinical and pathological aspects of 672 cases of influenza treated in the Fairfield Hospital, Melbourne, during July and August 1957. 169 patients had uncomplicated influenza, 127 had laryngotracheobronchitis (75% being under 9 years old) and 376 had pneumonia. 38 patients died; of these 4 had no evidence of pneumonia but had pre-existing serious disease, the other 34 all had pneumonia, and of these 19 had pre-existing chronic disease. The pneumococcus was the commonest cause of pneumonia, followed by the haemolytic streptococcus. Staphylococci appeared to be the sole cause in only 2 cases.

A. B. Christie

STILLE, W. T., WOOLRIDGE, R. L. & GUNDELFINGER, B. F. **Antibody Response to Intracutaneous and Subcutaneous Influenza Vaccination.** *J. Lab. & Clin. Med.* 1959, May, v. 53, No. 5, 751–4, 1 fig.

Antibody responses following the subcutaneous or intracutaneous administration of varying doses of an Asian influenza vaccine were determined by the haemagglutination-inhibition technique. With vaccine doses lower than 50 chicken cell agglutinating (CCA) units, antibody responses were higher among volunteers vaccinated by the intracutaneous route. The opposite was observed with vaccine doses higher than 50 CCA units.

It is suggested that variations in vaccine potency may explain the conflicting results of previously reported studies comparing different routes used for vaccination against influenza [this *Bulletin*, 1947, v. 22, 440; 1949, v. 24, 1013; 1958, v. 33, 729].

H. G. Pereira

JACKSON, G. G. & DOWLING, H. F. **Transmission of the Common Cold to Volunteers Under Controlled Conditions. IV. Specific Immunity to the Common Cold.** *J. Clin. Investigation.* 1959, May, v. 38, No. 5, 762–9, 1 fig. [16 refs.]

Immunity to the common cold was investigated by studying the clinical reactions of volunteers given

repeated intranasal doses of common cold nasal secretions. 5 different secretions collected in successive years from 1953 to 1957 were used. Volunteers were not kept in isolation and the results were based on the proportions of subjects showing objective and subjective signs of common cold among groups given infectivity and control materials. Among 1,034 volunteers given an initial dose of infectious secretions, 42% developed colds. This was contrasted with an incidence of 10% colds among a comparable group of 696 volunteers observed as controls. After a second dose of a given secretion, colds were observed in 10% (7 of 73) of volunteers with no cold after the primary dose and in 8% (6 of 71) of those who developed colds after the primary dose. The interval between the 2 doses varied from 3 to 45 weeks. The incidence of colds among volunteers given a different secretion 10 to 74 weeks after the first dose was of 40% among 74 subjects who developed no cold after the first dose and of 46% among 41 of those who did develop colds after the first dose.

It is suggested that the common cold is caused by several antigenically different viruses and that infection by a given common cold virus results in specific resistance lasting up to 45 weeks. *H. G. Pereira*

Liu, C., Eaton, M. D. & Heyl, J. G. **Studies on Primary Atypical Pneumonia. II. Observations concerning the Development and Immunological Characteristics of Antibody in Patients.** *J. Exper. Med.* 1959, June 1, v. 109, No. 6, 545–56, 1 fig. [16 refs.]

"By using the indirect method of fluorescent staining to study the antibody response in patients with primary atypical pneumonia associated with the development of cold agglutinin, it was found that the PAP antibody developed during the 2nd and 3rd week of the illness, and persisted for over a year, and is not related to the cold and streptococcus MG agglutinins. The development of the PAP fluorescent staining antibody paralleled the neutralizing antibody for the PAP virus as tested in cotton rats. The sensitivity of this specific serological test was indicated by the observation that 67 to 92 per cent of the patients in several outbreaks of PAP showed a rise of antibody titer during convalescence. Absorption of the sera with various tissue powders did not affect the PAP antibody detected by this method."

Goret, P. & Fontaine, M. Pneumopathies virales animales. Leurs rapports avec les pneumopathies virales humaines. [**Viral Pneumonias in Animals and their Relation to Viral Pneumonias in Man**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Apr.–May, v. 7, No. 3, 303–20. [Numerous refs.]

Elmes, P. C., Dutton, A. A. C. & Fletcher, C. M. **Sputum Examination and the Investigation of "Chronic Bronchitis".** *Lancet.* 1959, June 13, 1241–4.

In a survey of respiratory symptoms by questionnaire among groups of the working population of London, the validity of answers concerning expectoration was checked by an examination of specimens of sputum obtained in the hour after waking from the people who gave the answers. 144 postmen and 144 women sorters cooperated; half of each group were aged 40–49 years and half 50–59.

The study revealed that about half the men and a quarter of the women were in the habit of expectorating, and that purulent sputum was produced by a quarter of the men and an eighth of the women—indicating persistent bronchial disease, probably chronic bronchitis. Tubercle bacilli were found in 1 specimen from the 288 subjects. Those who produced more than 4 ml. sputum had a reduced indirect maximal breathing capacity, and a greater incidence of illness.

Sputum collection is judged to be useful adjunct to the method of survey by questionnaire.

H. Stanley Banks

Zhumatov, K. Z. & Dardik, F. G. **A Water-Borne Outbreak of Infective Hepatitis.** *Problems of Virology.* London. 1958, v. 3, No. 1, 37–41, 2 figs. [Translated from Russian.]

An outbreak of 2,676 cases of infective hepatitis between August 1955 and January 1956 occurred among the inhabitants of Kazan, U.S.S.R., where students were working on the cotton harvest. The main incidence (61·4%) was found in the age-group 16–40 years. The aged were also frequently affected (rate 107 per 10,000 persons over 40 years of age).

Enquiries showed that the cause was the use of unboiled drinking water from an irrigation canal, which was the only source of water supply. The disease was absent from one village where it was the habit to drink only tea; and among children in institutions, where the drinking water was boiled, the incidence was low compared with that among children living at home. In one hostel where 27 cases occurred during September, and compulsory boiling of water was then introduced, no further cases occurred during the whole period of the outbreak. A characteristic feature of a water-borne outbreak of infective hepatitis is said to be the comparatively frequent infection of the elderly [see, however, Kheifets *et al.*, below]. *H. Stanley Banks*

Kheifets, L. B., Kamolikova, T. L. & Kantorovich, R. A. **An Outbreak of Infective Hepatitis in an Arctic Settlement.** *Problems of Virology.* London. 1958, v. 3, No. 1, 48–50, 1 fig. [Translated from Russian.]

An outbreak of 74 cases of infective hepatitis occurred in a remote Arctic settlement at the end of 1955 and the beginning of 1956. The relatively large number of cases could not be explained solely by contact infection. There were 2 sources of water supply: (1) a reservoir, which was found to have a high degree of faecal contamination, and was associated with 47 cases, and (2) river water, a relatively pure source associated with 17 cases. The source of the outbreak was clearly the contaminated water supply, but a considerable part was played by contact infection, especially in schoolchildren.

Among the special features of the outbreak was the preponderance of abortive forms of the disease (ratio

of anicteric to icteric cases 1·7 to 1). The highest incidence was among schoolchildren (34 cases), and the lowest among adults (15 cases).

H. Stanley Banks

KACZMARECK, H. Serumeiweiss und Virushepatitis. [**Serum Protein and Virus Hepatitis**] *Ztschr f. ärztl. Fortbildung.* 1959, Jan. 25, v. 53, No. 2, 125–38, 6 figs. [Numerous refs.]

An investigation has been made of the serum protein content in 80 patients suffering from acute virus hepatitis. The percentage of the various fractions was determined by paper electrophoresis with subsequent elution and photometric determination, and the results were compared with those of a similar investigation carried out on the sera of 25 normal persons. The changes in the serum protein content were dependent on the duration of icterus; they were greatest in 11 patients in whom icterus had been present for 6 weeks or longer, with an increase of 18·77% in albumin, 4·36% in beta globulin and 13·24% in gamma globulin content. There was no significant change in the alpha globulin content.

D. J. Bauer

WANG, San-Pin & GRAYSTON, J. T. **Goat Red Blood Cells in Agglutination Test for Infectious Mononucleosis.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 111–13.

In Formosa, sheep can only be maintained with difficulty because of fluke infection. The possibility of using goat cells for the Paul-Bunnell test was therefore explored. In 100 normal sera, and in 61 sera from patients suspected to be suffering from glandular fever, the heterophil agglutinin titre when goat cells were used was fairly constantly 4 times that recorded when sheep cells were used. Nevertheless, "negative" sera, *i.e.* those with a sheep cell titre of 1 in 28 or less, and showing no agglutination after absorption with guinea-pig kidney, although they gave titres of up to 1 in 112 with goat cells, gave negative results with goat cells after absorption with guineapig kidney. Thus goat cells reacted with the same specificity as sheep cells, the only difference being in their four-fold sensitivity.

Alan B. Raper

JOHNSON, A. J., AYVAZIAN, J. H. & TILLETT, W. S. **Crystalline Pancreatic Deoxyribonuclease as an Adjunct to the Treatment of Pneumococcal Meningitis.** *New England J. of Med.* 1959, Apr. 30, v. 260, No. 18, 893–900, 2 figs. [23 refs.]

25 patients were treated with intravenous and intramuscular penicillin in doses of 12,000,000 to 40,000,000 units daily: 6 patients had 5,000 to 10,000 units intrathecally in addition on the first day. Crystalline pancreatic deoxyribonuclease was used in each patient intrathecally for the first 2 to 3 days in doses from 50,000 to 1,000,000 units daily. To patients with cerebrospinal fluid blocks, deoxyribonuclease was also given intravenously and intramuscularly. Deoxyribonucleic acid found in exudates consists mainly of highly polymerized saline-insoluble deoxyribonucleoprotein which is poorly absorbed by arachnoid villi and is capable of obstructing the flow of cerebrospinal fluid. The pancreatic enzyme depolymerizes this protein into smaller, saline-soluble dialysable fragments. Of the 25 patients, 3 died, a mortality of 12%: in a previous series treated similarly but without the pancreatic enzyme 24 of 64 patients died, a mortality of 37·5%.

A. B. Christie

GLUSCHENKO, P. A., GUTSEVICH, A. V. & DUDKINA, M. S. [**Investigation of Mosquitos as Vectors of the Virus of Lymphocytic Choriomeningitis in the Western Ukraine**] *Dokl. Akad. Nauk SSSR.* Moscow. 1957, v. 113, No. 5, 1181–3. [In Russian.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1959, May, v. 47, Pt. 5, 70–71.]

"The virus of lymphocytic choriomeningitis has been found to be transmitted by Gamasoid mites in the Soviet Union and by the bite of *Aëdes aegypti* (L.) in the laboratory elsewhere [*R.A.E.*, B **32** 62]. Investigations on the possible part played by mosquitos in the circulation of the virus in nature were made in the western Ukraine in 1956. Mosquitos were captured in wooded environments, far from centres of habitation, in July-August, when temperatures were high and would therefore favour multiplication of viruses, and since mosquitos are not known to transmit viruses through the egg, the selection of examples that had passed through at least one gonotrophic cycle was desired. This was done by observations on the cessation of adult emergence from breeding places and subsequent classification of samples according to their physiological age [**34** 180, etc.]. Since adults of some species of *Aëdes* are difficult to identify after they have lost part of the scales from the thorax and wings, mosquitos of such species were assigned to groups. The group of *A. communis* (Deg.) consisted of 70 per cent. *A. diantaeus* H., D. & K., 20 per cent. *A. sticticus* (Mg.), 9–10 per cent. *A. punctor* (Kby.) and a few examples of *A. communis* itself, and the group of *A. maculatus* (Mg.) comprised 95 per cent. of that species and 5 per cent. of *A. excrucians* (Wlk.). Suspensions were prepared from batches of not more than 50 mosquitos and injected intracerebrally into white mice. At least four passages were made, and mice of the fourth passage were observed for three weeks, after which the final results were drawn up. In all, 43 batches of mosquitos were investigated, and the final results showed that 13 strains of the virus were isolated from 30 batches of the group of *A. communis*, comprising 1,442 examples, two from four batches of the group of *A. maculatus*, comprising 130 examples, two from four batches of *Mansonia richiardii* (Fic.), comprising 113 examples, one from two batches of *A. cinereus* Mg., comprising 99 examples, one from a batch of 50 examples of *A. geniculatus* (Ol.), and none from a batch of 40 examples of *A. vexans* (Mg.) or one of 50 examples of *Anopheles claviger* (Mg.) (*bifurcatus*, auct.). Two of the strains were isolated from *M. richiardii* and the group of *Aëdes communis* in the originally infected mice, and the remainder during the first, second or third passage. All the strains caused death of the mice in 5–6 days, with typical symptoms of lymphocytic choriomeningitis.

"In 1954, the first author isolated a strain of virus (17-MK) from *Ixodes ricinus* (L.) that was identified from its immunological properties as the virus of lymphocytic choriomeningitis. The ticks were collected in the same districts as the mosquitos, and it is therefore concluded that mosquitos, ticks and mites are vectors of the virus and play a part in its circulation."

PATTYN, S. R., DELVILLE, J. P., VANDEPUTTE, M. & PEEL, J. J. Epidémiologie des virus entériques en Afrique. Etat actuel de nos connaissances. [**Present Knowledge of the Epidemiology of Enteric Viruses in Africa**] *Ann. Soc. Belge de Méd. Trop.* 1959, Feb. 28, v. 39, No. 1, 105–21, 2 charts. [19 refs.]

The English summary appended to the paper is as follows:—

"After the 1919–1920 epidemic, poliomyelitis was only sporadically seen until the second world war, when the disease reappeared. The necessity is emphasized for comparative epidemiologic research in infectious hepatitis in Africa, a virus disease which also has a fecooral transmission. The first results are given of the search for enteric viruses in healthy children in Leopoldville and Elisabethville. High rate of Polio virus infections in Leopoldville. Coxsackie virus infections were extremely common in both cities. Adenovirus infections are common. Although the poliomyelitis-epidemics invariably occur during the rainy, seasons, which correspond to the summer in the southern hemisphere, no significant quantitative differences could be demonstrated along with the various seasons. But only quantitative data are available at this moment, since too many isolated strains remain to be identified."

REEDY, J. J. **Recessive Inheritance of Susceptibility to Poliomyelitis. In Fifty Pedigrees.** *J. Heredity.* 1957, Jan.–Feb., v. 48, No. 1, 37–44, 3 figs.

"Pedigrees were compiled for 50 poliomyelitis patients. The pedigrees embrace 5,677 persons and include 153 cases of poliomyelitis, of which 115 were positive and 38 suspected.

"The frequency of poliomyelitis among the relatives of the 50 propositi in a specified five-year period was calculated to be 6.75 per 1,000 while the corresponding rate in the general population of that area was under two per thousand during the same period.

"Over 40 percent of all sibships containing paralytic poliomyelitis showed a familial history of secondary cases occurring in sibships having a coefficient of relationship of $\frac{1}{8}$.

"Sibship analysis showed that all of the data were consistent with an hypothesis of a single autosomal recessive gene as the basis of susceptibility to poliomyelitis.

"On the basis of the data of this study, the hypothesized gene for susceptibility to poliomyelitis has a penetrance on the order of 80 percent.

"The difference in incidence of poliomyelitis among males and females is not statistically significant, hence sex-linkage and sex-influenced patterns of inheritance are ruled out. Y-linkage is ruled out by the common occurrence of the disease in females.

"The data were not adequate to distinguish any genetic difference between bulbar and spinal types of poliomyelitis."

FARO, S. N. **Recurrent Paralytic Poliomyelitis. Report of a Case, documented with Virus Isolations.** *New England J. of Med.* 1959, June 4, v. 260, No. 23, 1177–8.

"A child at age three suffered a mild but characteristic attack of paralytic poliomyelitis due to Type 3 virus, and eleven months later a more severe attack of paralytic poliomyelitis proved to be due to Type 1."

STEVENS, K. M. **Estimate of Molecular Equivalents of Antibody required for Prophylaxis and Therapy of Poliomyelitis.** *J. Hygiene.* 1959, June, v. 57, No. 2, 198–201. [15 refs.]

The author [this *Bulletin*, 1958, v. 33, 411] has previously described a method of converting neutralizing titres of poliovirus antibodies into molar equivalents of antibody. It is calculated that 1×10^{-16} moles per litre of antibody were protective in the trial of gamma globulin carried out in the United States by HAMMON *et al.* [*ibid.*, 1953, v. 28, 690]. This, as Stevens points out, is an extremely small quantity; even such biologically active substances as atropine, colchicine and penicillin require from 10^{-8} to 10^{-6} moles for demonstrable activity in man. From the work of LIU *et al.* [*ibid.*, 1958, v. 33, 892; 1959, v. 34, 738] it is calculated that about $1{\cdot}5 \times 10^{-15}$ moles per litre of poliovirus neutralizing antibody in the cerebrospinal fluid halted the progress of poliomyelitis in monkeys. Although this is a small amount the impurities present in gamma globulin which is calculated to contain only 1 part of specific antibody in 10^8 to 10^9 parts of globulin necessitates a very large dose of gamma globulin in order to have a therapeutic effect. On this basis the failure of COLIO *et al.* [*ibid.*, 1958, v. 33, 823], who gave 10 ml. of rabbit gamma globulin containing poliovirus neutralizing antibodies in high titre intramuscularly to a patient with poliomyelitis, to affect the course of the disease, is understandable. Supposing all the antibody had reached the cerebrospinal fluid it was calculated that about 7×10^{-16} moles per litre would be present in the cerebrospinal fluid which is less than the level found by Liu *et al.* to be effective in monkeys.

A. J. Beale

BARRETT, C. D., Jr., TIMM, E. A., MOLNER, J. G., WILNER, B. I., FAHEY, Martha F. & MCLEAN, I. W., Jr. **Multiple Antigen for Immunization against Poliomyelitis, Diphtheria, Pertussis, and Tetanus. II. Response of Infants and Young Children to Primary Immunization and Eighteen-Month Booster.** *Amer. J. Pub. Health.* 1959, May, v. 49, No. 5, 644–55, 6 figs. [25 refs.]

There is increasing interest in the incorporation of poliovaccine in a comprehensive scheme for immunizing

children. In order to do this the response of young children to poliovaccine and the effect of combining poliovaccine with other prophylactics must be determined. In this paper a study of the use of Quadrigen, a Parke Davis antigen containing poliovaccine, diphtheria and tetanus toxoids and pertussis vaccine with 2–2·5 mgm./ml. of aluminium phosphate, is presented. The vaccine was administered in 4 doses each of 0·5 ml. at monthly intervals to children under 6 months and in 3 doses also at monthly intervals to children between 6 months and 5 years. 18 months later a booster dose was given. The response to all antigens for all the children was excellent after the booster dose. The children under 6 months responded less well to poliovaccine, there was no change in the median antibody level after 3 doses, but after a fourth dose (when, of course, the children were over 6 months) the response was as good as in the older children. 76 children who were triple negative completed a primary course and 89%, 98% and 69% responded to Types 1, 2 and 3. The antibody levels before the booster dose of vaccine were fairly well maintained for the whole group of children. 75%, 95% and 55% of children still had antibodies to Types 1, 2 and 3 poliovirus over 1 in 4. The response to the booster dose was excellent, 100% responding to Type 1 and over 95% to the other 2 types. The response to the other antigens in the vaccine was also excellent.

[For Part I, see this *Bulletin*, 1958, v. 33, 1112.]

A. J. Beale

BARON, S., BARNETT, E. V., BURCH, Beatrice L., LYNCH, J. M. & EHRMANTRAUT, W. R. **Rapid Immunization with Poliomyelitis Vaccine.** *New England J. of Med.* 1959, May 7, v. 260, No. 19, 966–9, 3 figs. [28 refs.]

The authors note that poliovaccine given in a 3-dose schedule over 3 or 7 months prevents poliomyelitis. They were concerned as to how to boost immunity rapidly in the face of an epidemic. It was found that multiple doses at weekly intervals did not produce a rapid rise in antibody levels. However, 1 10 ml. dose into the gluteal muscles was found to be very effective. The response 14 days after 1 ml. or 10 ml. of commercially available vaccine in adults is shown in the table.

Type	Dose ml.	No. Responding/ No. inoculated	Geometric mean titre in responders
1	1	2/11	10
	10	10/12	70
2	1	9/10	50
	10	6/7	500
3	1	1/10	10
	10	7/8	90

The 10 ml. dose was well tolerated and there was no evidence of sensitization to penicillin, or of renal damage. The procedure is considered safe and likely to be effective in the face of a threat of poliomyelitis.

A. J. Beale

PELNER, L. **Allergic Reaction to Poliomyelitis Vaccine probably due to Penicillin.** *New England J. of Med.* 1959, Jan. 29, v. 260, No. 5, 230–33. [12 refs.]

Instances from the literature are cited to show that major allergic symptoms, some fatal, can be produced in penicillin-sensitive subjects by contact with the most minute quantities of penicillin. An illustrative case is described—a man of 28 who developed malaise, giant urticaria, fever, lymphadenopathy, exfoliative dermatitis and jaundice after an injection of Salk-type poliomyelitis vaccine, which usually contains a minute amount of penicillin. An exception is the vaccine produced by Wyeth Laboratories which is reconstituted with polymyxin B instead of penicillin. This brand was used for the patient's second injection of poliomyelitis vaccine, and there was no incident or sequel of any kind.

H. Stanly Banks

HALE, J. H., DORAISINGHAM, M., KANAGARATNAM, K., LEONG, K. W. & MONTEIRO, E. S. **Large-Scale Use of Sabin Type 2 Attenuated Poliovirus Vaccine in Singapore during a Type 1 Poliomyelitis Epidemic.** (With an addendum on Data on Large Lots of Live Attenuated Type 2 Poliovirus Vaccine distributed by A. B. SABIN.) *Brit. Med. J.* 1959, June 20, 1541–9. [13 refs.]

This important paper records the results of the laboratory control of the use of attenuated Type 2 poliovirus in the face of a Type 1 poliomyelitis epidemic. In August 1958 Singapore experienced its first serious epidemic of poliomyelitis. There were 415 cases, about 20% over 6 years of age. The incidence was about 3 times higher in Europeans but was equally prevalent in Chinese, Malays, Indians and Eurasians. There had been warning signs of an epidemic; the infant mortality fell to around 80 from 1949 onwards and a serological survey in 1956 showed that 50% of children had antibodies to the individual types of poliovirus by 3 years. Because of these facts it was decided to offer the population attenuated poliovirus on a voluntary basis. Sabin's Type 2 virus was used in the face of the epidemic due to Type 1 for 2 main reasons.

1. *Safety.* The spread of Type 2 virus would be detectable in a type epidemic as would disease due to this type.
2. *Protection.* Although the experiment was not designed to assess protection the Type 2 vaccine might protect by 2 mechanisms: (a) by interference with the growth epidemic Type 1 virus in the gut, which might confer protection on the individual and by limiting Type 1 virus viral excretion protect the community;

(b) by heterologous immunity since people with Type 2 antibodies are probably partially protected against Type 1 virus also.

The experiment yielded the following results:

Safety. The vaccine was given to 198,965 children under 10 years, and none of these children developed any illness attributable to Type 2 poliovirus. The virus spread freely in the community, thus before the

experiment 7 out of 248 children excreted Type 1 poliovirus and none Type 2, whereas after vaccination 23 out of 633 non-vaccinated healthy children excreted Type 1 virus and 14 Type 2 virus. Only 1 case of poliomyelitis due to Type 2 poliovirus was discovered in a non-vaccinated child. Since Type 2 poliovirus was known to be circulating on the mainland, though not proved to be in Singapore itself, because the neuropathogenicity of wild Type 2 viruses was greater than that of excreted vaccine virus and because only 1 case occurred, the authors do not ascribe this case to the vaccine. Virus excreted from vaccinated children or contacts was of greater pathogenicity for monkeys than the vaccine virus, but probably not as great as wild-type virus.

Efficacy: (a) *Establishment of Infection.* A serological survey before the commencement of the trial showed that immunity to Type 1 virus was at a higher level than in 1956. (The survey was carried out when the epidemic was already 12 weeks old.) Almost one-half of the children under 3 lacked Type 1 antibodies and the great majority of these also lacked Type 2 antibodies. The proportion of vaccinated children found to be excreting Type 2 poliovirus in each age-group was closely similar to the proportion lacking Type 2 antibodies. Since Sabin has reported that enteric virus infection may interfere with the establishment of infection with attenuated poliovirus, a survey of faecal excretion was carried out before the experiment began. 18% of the children under 6 excreted a virus other than polio and nearly 3% a Type 1 poliovirus but these viruses did not appear to interfere with the vaccine virus. Sera from 68 out of 71 children over 2 years who lacked antibodies to Type 2 virus before vaccination contained them afterwards. 45 out of 54 children under 2 years responded to the Type 2 vaccine.

(b) *Protection.* The experiment was not designed to assess the protective effect, and vaccine was made freely available on a voluntary basis. The composition of the vaccinated and unvaccinated groups is not assessed. Similarly, the fact that the attenuated Type 2 virus spread through the community made a separation of vaccinated from unvaccinated impossible. There were 16 cases of poliomyelitis in the vaccinated group but only 6 of these had their onset over 8 days after vaccination and none during the period of 10–20 days when the effect of Type 2 virus interference might be expected to be maximal. In the same period there were 179 cases in a population of about 300,000 unvaccinated children. Since many of these children would be vaccinated and probably protected by contact, the authors consider the real figures might be even more impressive. However, if a child developed poliomyelitis before being vaccinated it would be included in the control group. 2 weeks after the last vaccination there were 13 cases, all in non-vaccinated children.

[The authors are to be congratulated on the prompt appearance of the results of this trial which clearly involved an immense amount of work. Another paper is promised on the organization of the vaccinations. It is to be hoped that this will contain an analysis of the composition of the vaccinated group. It is stated that the age distribution in the vaccinated and unvaccinated groups was similar. If proportionately more children of 4–10 had been vaccinated than children up to this age then, since over 90% of the cases occurring after the vaccine programme began and all the vaccine failures were under 4 years, the comparison between vaccinated and unvaccinated attack rates might be much less impressive than the crude figures.]

A. J. Beale

DAIKOS, G. K., GARZONIS, S., PALEOLOGUE, A., BOUSVAROS, G. A. & PAPADOYANNAKIS, N. **Benign Myalgic Encephalomyelitis. An Outbreak in a Nurses' School in Athens.** *Lancet.* 1959, Apr. 4, 693–6, 2 figs. [13 refs.]

In May and June 1958 an outbreak of benign myalgic encephalomyelitis occurred in a school for midwives in Athens, presenting with obscure neurological illness of similar patterns to that observed among the Royal Free Hospital nursing staff in London, and in numerous other outbreaks among nursing staffs in Europe and America since 1950 [see, for example, this *Bulletin*, 1957, v. 32, 834; 1958, v. 33, 16]. There were 27 cases, 25 in the school and 2 in neighbouring institutions, all young female adults. The main symptoms were muscle pains (in 100%), subjective sensory disturbances (74%), headache (67%), muscular contractions (52%), mild pyrexia (44%), and in diminishing incidence loss of appetite, neck stiffness, photophobia, double vision, and gastrointestinal symptoms. The more common signs elicited were tenderness at the periosteum, tender sheaths, and periarticular tissues, sometimes accompanied by swelling of joints (a feature peculiar to this outbreak and present in 74% of the patients), abnormal tendon reflexes, usually brisk (63%), objective sensory disturbances (55%), equivocal plantar response, never extensor (48%), pareses (44%). The cerebrospinal fluid was normal in the 4 patients in whom it was examined. Mild psychic disturbances were prominent, and in 4 patients these were rather serious, though transient. Electromyography showed a typical pattern in 4 of 6 patients examined—reduction in the number of motor unit potentials (30–35 cycles/second), and grouping of these potentials. The electroencephalogram was highly abnormal in 1 of 4 patients examined. Relapses were not uncommon but the eventual outcome was good.

The main features were thus intense muscle pains, slight and transient pareses, extreme tenderness at periosteum and periarticular tissues, mental disturbances, and objective evidence of diffuse involvement of the central nervous system.

H. Stanley Banks

HILL, R. C. J., CHEETHAM, R. W. S. & WALLACE, H. L. **Epidemic Myalgic Encephalomyelopathy. The Durban Outbreak.** *Lancet.* 1959, Apr. 4, 689–93, 2 figs.

Another outbreak of the same, or similar disease [see above] occurred among the nursing staff of Addington Hospital, Durban in February and March 1955, and it spread sporadically to the city and its suburbs. There were 98 members of the nursing staff affected, the age range being 17–49 and the majority under 25. The incidence of sequelae was greater in the older age-groups. In the 30 cases diagnosed outside the hospital

the age range was 15–54. No children were known to be affected.

The syndrome had a superficial resemblance to poliomyelitis (of which there was an epidemic at the time), but it was essentially similar to that of the recent outbreaks in many parts of the world designated latterly as benign myalgic encephalomyelitis. It was characterized by diffuse involvement of the central nervous system associated with myalgia, a tendency to relapse, occasional permanent sequelae, and psychiatric concomitants often resembling hysteria. It was probably an acute infection, as suggested by the mild pyrexia, systemic symptoms and signs, and case-to-case spread. In the absence of significant pathological change in the cerebrospinal fluid at any stage of the illness, the authors prefer the term "encephalomyelopathy" to "encephalomyelitis". The illness showed a predilection for the female staff of a closed community, although it also occurred sporadically among the general population.

[For a preliminary account, see also this *Bulletin*, 1955, v. 30, 1047.] *H. Stanley Banks*

LIPTON, M. M. & STEIGMAN, A. J. **Allergic Encephalomyelitis. The Extraction of Highly Active Fractions from Bovine Spinal Cord.** *J. Immunology*. 1959, May, v. 82, No. 5, 409–14, 1 fig.

"1. By extraction of whole moist bovine spinal cord with petroleum ether, a fraction can be obtained which is highly encephalitogenic when combined with Freund adjuvants and injected intracutaneously into guinea pigs.

"2. Fractionation with acetone, chloroform and methanol yields a preparation which causes a high rate of allergic encephalomyelitis when injected in 5-γ amounts. This material contained 6.3% nitrogen.

"3. Further fractionation yields a fraction (almost completely protein) which is found to be highly encephalitogenic in 2-γ amounts."

TAYTSCH, Zofia F. & WRÓBLEWSKA, Zofia. Badanie naturalnego ogniska zapalenia mózgu w Puszczy Białowieskiej. [**Investigation of a Natural Focus of Tick-Borne Encephalitis in Bialowieza National Park**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 4, 339–53, 2 charts. [16 refs.] English summary.

In an investigation of a focus of tick-borne encephalitis infection in Białowieża National Park in Poland carried out in 1954–6, 2,254 rodents and insectivores belonging to 20 species were caught in the area and examined for the presence of the virus. In 1955 strains of tick-borne encephalitis virus were isolated from 22 of 259 pools of 5 to 10 brains from 2,254 animals, and from 13 of 88 pools of 2–3 blood samples, and in 1956 10 strains of virus were isolated from 44 pools of brains from 192 animals. Among the animals infected were *Clethrionomys glareolus*, *Apodemus flavicollis*, *Sorex araneus*, *S. minutus* and *Microtus* sp. In 1955 the virus was also isolated from 8 of 120 batches comprising a total of 17,000 arthropods (*Aëdes*, *Anopheles* and *Ixodes ricinus*) and from 7 of 73 batches in 1956. Complement-fixing antibody was found in the sera of 17 of 128 (13·2%) cows in the area, less frequently in other domestic animals and small wild mammals, and in the sera of 35% of 32 forest workers.

D. J. Bauer

LACHMAJER, Jadwiga, SKIERSKA, Barbara & WEGNER, Zofia. Wstepne dane o roli stawonogów pasożytniczych w ognisku kleszczowego zapalenia mózgu w Białowieży w latach 1955–1956. [**Preliminary Data on the Rôle of Arthropods in a Focus of Tick-Borne Encephalitis obtained in Bialowieza in 1955–56**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 4, 355–62, 3 charts. [18 refs.] English summary (9 lines).

In 1955–6 an investigation was made of the mosquito and tick fauna of a focus of tick-borne encephalitis infection in the Białowieża National Park in Poland. The numbers of ticks (*Ixodes ricinus*) were greatest in May and June, and the greatest numbers of mosquitoes (*Aëdes* spp., *Anopheles* spp.) were caught in July. The virus could be isolated from various developmental stages of *I. ricinus*, both caught in the open and taken from cows, and the maximum incidence of human cases occurred shortly after the period of maximum activity of the ticks. It was also possible that mosquitoes might participate in the transmission of the disease.

D. J. Bauer

KOZŁOWSKI, S. & ŻUKOWSKI, K. Badania nad pasożytniczymi Gamasides Białowieskiego Parku Narodowego. [**Investigations on Parasitic Gamasides in Bialowieza National Park**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 4, 363–8. [19 refs.] English summary.

An examination has been made of gamasid mites caught in 1955–6 on wild rodents and insectivores inhabiting an endemic focus of tick-borne encephalitis in the Białowieża National Park in Poland. 17 species were identified, the most frequent being *Laelaps agilis* and *Haemogamasus nidi*; all had previously been recorded from Central Europe. The authors regard gamasid mites as possible vectors of tick-borne encephalitis virus, although attempts by other investigators [see above] to isolate the virus from the Gamasids have been unsuccessful. *D. J. Bauer*

KICINSKA, Halina. Badania nad epidemiologią kleszczowego zapalenia mózgu w województwie białostockim. [**Epidemiological Investigations on Tick-Borne Encephalitis in Bialystok Province**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 4, 373–84, 2 charts. [23 refs.] English summary.

Investigations have been made of the epidemiology of tick-borne encephalitis in 1954–6 in the province of Białystok in Poland, which includes the focus of endemic infection in the Białowieża National Park. In an examination of records of 7 hospitals situated in the area 86 cases were detected in which the features of the illness were consistent with a retrospective diagnosis of tick-borne encephalitis. The main incidence (61 cases) was in May–July and most cases had originally been diagnosed as bacterial meningitis. In 1956 20 patients

suffering from possible tick-borne encephalitis were examined in hospital; the diagnosis was confirmed virologically in 7 instances. The incubation period ranged from 4 to 14 days and contact with ticks could be established in 7 instances. *D. J. Bauer*

CHINESE MED. J. Peking. 1959, May, v. 78, No. 5, 419–23. **Artificial Hibernation in Treatment of Epidemic Encephalitis Type B.**

Epidemic encephalitis due to the Japanese B virus is widespread throughout China in summer and autumn, causing in the past a case mortality of the order of 35% among the childhood population. Even streptomycin therapy, which had proved the most effective to date, reduced the mortality rate in 210 cases only to 15·7%. The authors have endeavoured to reduce this further by the use of artificial hibernation and here record a strikingly successful result, since among 28 consecutive patients so treated only 2 (7·1%) died, the rest making complete recoveries.

The children treated ranged in age from infancy to 14 years: the ratio of males to females was 4 : 3. All but 4 patients were severely ill, with fever, convulsions and coma, nuchal rigidity, positive Kernig's sign and extensor plantar responses. In 23 patients the cerebrospinal fluid showed a pleocytosis in excess of 50 leucocytes per cmm., and in 22 there was an excess of globulin. The majority of the children were admitted to hospital after the third day of their illness.

The basis of hibernation treatment was cooling of the whole body surface with ice-bags under sedation induced by intravenous chlorpromazine. If the patient was in coma on admission, after establishment of the diagnosis, treatment was initiated by the setting-up of a continuous intravenous drip transfusion through which was administered 500 ml. of a 5% solution of glucose in half-normal [saline], to which was added novocain 0·5 gm., magnesium sulphate 1 gm. and vitamin BI 100 mgm. This was completed in 4 hours, after which chlorpromazine was introduced into the continuous glucose saline drip at a dosage of 5 mgm. every 2–4 hours. Cooling was begun 30–60 minutes later and was continued until the [? rectal] temperature had been reduced to "less than 36C". If difficulty was experienced in reducing the temperature [for reasons not stated], the initial infusion mixture was repeated. After 2 days hibernation chlorpromazine was withdrawn. The dosages set out above refer to patients below 5 years of age; older children received double the stated dosage of novocain, magnesium sulphate and chlorpromazine. Additional therapy included the use of penicillin, streptomycin, vitamins, butazone (40 mgm. per kgm. body weight) corticotrophin (2·5–5 mgm.), by injection, while 0·1% noradrenaline was given via the drip infusion whenever grave circulatory collapse threatened.

The results observed were as follows: consciousness returned in 3 days in 51% and in 5 days in 81% of patients, the duration of coma averaging 3·9 days with a range of 1 to 11 days. Among 52 comatose patients treated in 1955, before the introduction of artificial hibernation, 50% returned to consciousness in 3 days, 65% in 5 days, while the mean duration of coma was 7·5 days, with a range of 1–57. Under artificial hibernation the cerebrospinal fluid became normal after an average of 8·3 days, compared with the usual 15–30 days under conventional treatment.

The article attributes the success of hibernation treatment simply to the control of hyperpyrexia which is the immediate cause of death in patients managed conventionally. The only 2 fatalities in this series resulted from pharyngeal obstruction by accumulated secretions [and might presumably have been avoided].

[This paper reports a major therapeutic advance in the management of this dangerous disease.]

J. H. Walters

WISEMAN, J. S., GRIMES, J. E. & EADS, R. B. **St. Louis Encephalitis Outbreak in Cameron County, Texas.** *Mosquito News.* 1959, Mar., v. 19, No. 1, 3–7, 1 pl.

119 human cases occurred in the area in July–August 1957. The entomological investigations reported were made in early August. The outbreak occurred during a period of drought and at a time when irrigation was at a minimum. *Culex quinquefasciatus* [*fatigans*] was the predominant mosquito species found and was breeding particularly in water supply and sewage plants and in industrial waste waters. Septic tanks and their effluents were an important source. Adult mosquitoes were caught in daylight resting places such as chicken houses and calf sheds; light traps and the sweeping of vegetation with insect nets were also used. 85% of the 1,900 mosquitoes caught were *C. quinquefasciatus* and the next most numerous species (*Anopheles quadrimaculatus*) accounted for only 8%.

Mosquitoes were held alive for 24–48 hours so that blood meals would be digested, and were then ground up, treated with antibiotics and inoculated intracerebrally into mice. One blind passage was made where necessary. St. Louis encephalitis virus was isolated from 8 pools of *C. quinquefasciatus* collected in mid-August. The strains were identified by cross-neutralization tests. No isolations were made from 3,082 mosquitoes caught between December 1957 and April 1958 in the same area.

General opinion was that mosquito populations were low at the time of the outbreak, and sufficient numbers for an outbreak to occur were therefore present without being evident to the public or even public health personnel. Antibody studies indicated that inapparent infections greatly outnumbered clinical cases.

C. E. Gordon Smith

WALLIS, R. C. **Host Feeding of** *Culiseta morsitans.* *Proc. Entom. Soc. of Washington.* 1957, v. 59, No. 4, 199–200. [Summary taken from *Rev. Applied Entom.* Ser. B. 1959, May, v. 47, Pt. 5, 66–7.]

"The host-preferences of mosquitos that feed on birds in the eastern United States are important because of the part played by birds, and particularly pheasants, as reservoirs of eastern equine encephalitis [*cf. R.A.E.*, B **29** 38], but little information is available for many species. Special attention has recently been paid in Connecticut to species of *Culiseta,* in view of isolations

of the virus from *C. melanura* (Coq.) [*cf.* **45** 97] and in particular three from collections made in New Jersey near a pheasant pen. Adults of *C. morsitans* (Theo.) were collected regularly from diurnal resting places near a domestic pheasant pen in Connecticut in the early summer of 1956, and it was found that in the four-week periods before and after 14th July, when young pheasants were put in the pens, 2·6 per cent. of 115 females and 35·2 per cent. of 88 females examined, respectively, contained blood. Microscopic examination of smears from six blood-fed females showed that all contained nucleated red blood cells. The sharp increase in the number of females containing blood could not be connected with any change in the populations of wild birds or other potential hosts, or of the environment generally, other than the introduction of the pheasants. The proportion of engorged females caught during the first week after the pheasants became available was considerably higher than in the subsequent ones, and, although alternative explanations are possible, it is concluded that a population of females ready to feed had built up and that the young pheasants provided a suitable source of food. This is the first record of the finding of blood-engorged females of *C. morsitans*."

PARIKH, M. M. & THANAWALA, J. K. **Tetracycline in Enteric Fever.** *J. Indian Med. Ass.* 1959, Apr. 16, v. 32, No. 8, 316–22.

189 patients suffering from enteric fever were treated with varying doses of tetracycline, with tetracycline combined with chloramphenicol and with chloramphenicol followed by tetracycline: the results of treatment were compared with the results of chloramphenicol treatment. Tetracycline did not prove successful so consistently as chloramphenicol but when it did it appeared to reduce toxaemia and temperature more quickly. Chloramphenicol and tetracycline given together seemed to give better results than either drug given alone or following one another. [The figures given require to be studied with caution: dosage and time intervals differ in all the groups.]

A. B. Christie

KOPACKA, Bronisława. Badania nad hemaglutynacją w salmonelozach. [**Investigations on the Haemagglutination Test in** *Salmonella* **Infections**] *Przegląd Epidemiol.* Warsaw. 1958, v. 12, No. 4, 397–405. [24 refs.] English summary.

An investigation has been made of the diagnostic value of haemagglutination tests carried out with red cells sensitized with polysaccharide antigens obtained from 4 species of *Salmonella*. Titres of 200 or higher were obtained with 116 of 130 sera (89·2%) from patients suffering from typhoid in tests in which somatic antigen from *Salm. typhi* was used, compared with 95 (73·2%) positive results in Widal tests carried out in parallel. The haemagglutination test also gave a higher proportion of positive results than the agglutination test in the examination of the sera of 11 patients suffering from paratyphoid B and 8 suffering from illnesses due to *Salm. typhi-murium* and *Salm. cholerae suis*.

D. J. Bauer

FUKAYA, K., SUZUKI, M., ISHII, S., KAWASHIMA, A., ENOMOTO, K., TAKAYAMA, H. & KITAMOTO, O. **Kanamycin in Bacillary Dysentery.** *Japanese J. Exper. Med.* 1959, Feb., v. 29, No. 1, 37–43.

Since kanamycin possesses tuberculostatic properties comparable with those of streptomycin the authors decided to test its activity against the *Shigella* group of organisms, which are generally sensitive to the latter agent.

A group of patients suffering from acute dysentery due to *Shigella flexneri* types 2a, 2b and 3a formed their experimental subjects. *In vitro* experiments showed that the minimum inhibitory concentration of kanamycin was 7·1 microgrammes per ml. The therapeutic trial employed a daily regime for adults of 3 gm. orally (in 4 divided doses) or 4 gm. by intramuscular injection (in 2 doses) each for 5 days. Children received 3 gm. daily by mouth. The intramuscular route proved ineffective and painful and was abandoned. In an additional limited experiment the combined action of chloramphenicol 250 mgm. twice daily and kanamycin 750 mgm. twice daily was observed.

The clinical effect of kanamycin was considered to have been very good. The stools became free from shigella within 2–3 days, the inflammatory exudate cleared in the same period, though mucus might persist for a day or two longer. The fever abated on the 2nd or 3rd day. The specific pathogen reappeared, however, in the stools of 2 patients after treatment, though this rate of relapse was low compared with that after other forms of therapy.

2 troublesome side effects were encountered. The drug proved nauseating when taken in aqueous solution, though this was overcome by giving it in solid form "wrapped in the wafer" [this probably means enclosed in a rice-paper capsule]. Furthermore the drug itself appeared to cause diarrhoea [? by chemical irritation]. A further disadvantage, which, however, the authors considered to be of no practical importance, was the abolition of *Escherichia coli* from the bowel and the promotion of growth of *Proteus*, *Streptococcus faecalis* and *Candida albicans* in the stools.

The combination of chloramphenicol with kanamycin which was tested in 7 patients showed no advantage over the use kanamycin alone.

[This new antibiotic appears to offer no advantages over chloramphenicol or oxytetracycline in the treatment of *Sh. flexneri* infections. Little seems yet to be known as to its possible undesirable effects.]

J. H. Walters

LEPPÄNEN, M. K. **The Occurrence of** *Escherichia coli* **Serotypes 26 : B6, 55 : B5, 86 : B7, 111 : B4, 125 : B15, 126 : B16 and O Groups 44 and 78 in Inflamed and Healthy Appendices and Faeces.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1959, v. 37, No. 1, 105–9. [21 refs.]

This study was undertaken in order to discover whether those strains of *E. coli* found in association with infant gastro-enteritis were present in appendices (healthy or inflamed), peritoneal exudates, and faeces of

patients. From these sources 3,500 strains were examined from a total of 310 patients whose ages ranged from 2 to 74 years: the following serotypes were sought—O26 : B6, O55 : B5, O86 : B7, O111 : B4, O44 : L74, O125 : B15, O126 : B16 and O group 78. None of these strains was isolated from any of the specimens, except in 2 cases of appendicitis; both these patients were boys, aged 4 and 6 years, and from the faecal specimens only were isolated *E. coli* O55 and O86 respectively—no homologous antibodies were detected in the sera. The author concludes that his findings confirm the view that these "diarrhoeal" serotypes occur only in epidemic infantile diarrhoea.

John S. Stevenson

YOUNG, Viola M., WARREN, J. & LINDBERG, R. B. **Absence of Intestinal Viral Flora in Infants during Epidemic of *Escherichia coli* Gastro-enteritis.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 579–81. [16 refs.]

In an outbreak of gastro-enteritis involving 25 infants, *E. coli* O111 B4 was isolated from all but 2 of the patients, and in an attempt to discover whether or not a virus played any part in the pathology of the outbreak, specimens of faeces, 2 throat washings and one vomitus were studied as follows: the specimens were frozen with dry ice and within 4 weeks 10% suspensions were prepared in saline and centrifuged at 3,000 r.p.m. for 30 minutes: from the supernatant fluid, 3 inocula were prepared by (a) passing a portion through an ultrafine sintered glass filter, (b) recentrifuging a portion at 10,000 r.p.m. for 30 minutes at 4°C., (c) recentrifuging a portion at 30,000 r.p.m. for 1 hour at 4°C. In (c) the sediment was resuspended in saline and used as the inoculum. Each preparation was inoculated into mice, hamsters and fertile hens' eggs, and into monkey kidney and HeLa cell cultures. All these tests for the presence of a transmissible virus were negative, but it was found that sera from 2 of the patients gave strongly positive reactions when tested for the circulating antibody of *E. coli* O111 B4 by the haemagglutination-inhibition test. The authors conclude that this gastro-enteritis outbreak was caused by the type-specific strain of *E. coli*, and that other "microbial agents" played no part in the aetiology.

John S. Stevenson

ABOUL-DAHAB, Y. W., TAWIL, G. S. & EL-KHOLY, S. **Response to Infantile Gastro-enteritis to Chloramphenicol. The Variability as conditioned by the Spread of Resistant Strains of Serospecific *Escherichia coli* O20.** *J. Dis. Children.* Chicago. 1958, Sept., v. 96, No. 3, 348–61, 1 fig. [24 refs.]

This is a report of investigations, clinical and bacteriological, into acute gastro-enteritis occurring among infants treated in the departments of paediatrics, Abbassieh Faculty of Medicine. Patients were divided into 2 treatment groups, the one receiving chloramphenicol and the other succinyl-sulphathiazole. In the first phase of treatment the results were slightly more favourable in the chloramphenicol group (although there were more deaths) but in the third phase there was an outbreak of cross-infections and the chloramphenicol treated patients fared worse. The cross-infecting organism was a new strain *Escherichia coli* D48/11054, the somatic antigen of which belonged to sero-group O20: this organism was resistant to chloramphenicol. The authors feel that unless bacteriological investigation with antibiotic sensitivity tests can be carried out concurrently, the use of an antibiotic like chloramphenicol may when cross-infection occurs be more hazardous than beneficial. [This article includes much bacteriological detail which can only be studied in the original.] *A. B. Christie*

ROBERTS, W. & WOODGER, B. A. **Neomycin in the Control of Outbreaks of Infantile Gastro-enteritis.** *Scottish Med. J. Glasgow.* 1959, May, v. 4, No. 5, 228–31, 1 fig. [10 refs.]

In an attempt to assess the value of neomycin in the control of infant gastro-enteritis a ward of 15 babies was studied over 2 successive periods of 3 months. In the first period, babies requiring treatment were given either sulphadiazine or neomycin for 5 days. In the second period, all babies were given neomycin, 50 mgm. per kgm. body weight, daily throughout their stay up to 21 days. Faeces were examined daily for specific types of *Escherichia coli*. In the first period, when 86 babies were involved, there were 28 cross-infection incidents, as judged by the appearance of a new strain or the reappearance of an old one after an interval of 14 days. In the second period involving 97 babies, there were 4 such incidents.

In a ward for pneumonia with 19 patients, several had diarrhoea and *E. coli O*111 was found in the faeces in 6. The ward was not closed, as beds were in great demand, but all the patients, including 11 under 1 year of age, were given neomycin for 10 days: 4 of the babies excreting the organism had symptoms of gastro-enteritis and were removed from the ward; the other 2 remained in it. Children were discharged when well and new admissions were accepted. After the 10 days' treatment, all bacteriological tests were negative and there was no further evidence of infection.

The authors do not recommend the continuous prophylactic use of neomycin in gastro-enteritis wards but suggest that it may be useful in controlling outbreaks of gastro-enteritis. *A. B. Christie*

HOEKENGA, M. T. **Observations on Treatment on Infant Diarrhea in Panama.** *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 148–50.

Diarrhoeal diseases are the main cause of death in infants in Western Panama: enough work has not been done to elucidate the bacteriology of the condition but shigellosis and salmonellosis are probably not important. An attempt was made to assess the effectiveness on a clinical basis of 3 different preparations in 281 cases of infant diarrhoea: neomycin, succinylsulphathiazole and a mixture of streptomycin and neomycin in a base of carobtree powder (Intromycin). Of the total 20 were severely ill and were treated in hospital with Intromycin. All 3 preparations yielded good results with cure in

less than 48 hours in 74%, 79·5% and 88·1% (50% in the hospital cases). A related, but not comparable study in adults treated with a placebo, iodochlorhydroxyquin or neomycin showed equally good results for all 3, showing that diarrhoea in adults in this area is a self-limiting disease and should not be compared with the disease in infancy. *A. B. Christie*

ERRATUM

In the abstract of the article by VAL'VACHEV, N. I. & ROMANOV, B. G. (this *Bulletin*, 1959, v. 34, 614), reference is made to *Shigella boydii* type 3. This should read *Shigella boydii* type 4.

TUBERCULOSIS

LOGAN, W. P. D. **Tuberculosis Deaths and Un-Notified Cases.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, May, v. 18, 72–80.

In 1956 notifications of tuberculosis in England and Wales numbered 35,504 and deaths assigned to tuberculosis numbered 5,375. In addition there were several thousand more with mention of tuberculosis on the death certificate as a contributory condition. The total number of death certificates in 1956 mentioning tuberculosis included 1,465 of persons not on a tuberculosis register; this represents 27% of the total assigned deaths and 4% of the formal notifications.

A special enquiry was made into all deaths registered in England and Wales during October 1957 in which tuberculosis was mentioned to find out (a) if the present assignment of deaths to tuberculosis gives a proper statistical picture and (b) what proportion of cases are notified before death.

The diagnosis of tuberculosis was regarded as the responsibility of the certifying practitioner and no attempt was made to check its accuracy. Enquiries addressed to certifying doctors numbered 522 and 473 replies were received. These 473 deaths were classified: of the 280 deaths assigned to tuberculosis 189 were confirmed as directly due or probably due to tuberculosis, 68 due or probably due to a sequela of tuberculosis and 23 were not due to tuberculosis. The disease was regarded as active in 98, 63 and 57% respectively of these sub-groups.

Deaths not assigned to tuberculosis numbered 193 of which 12 were confirmed as due to tuberculosis, 29 as due to sequelae of tuberculosis and 152 as not due to tuberculosis. The disease was regarded as active in 100, 62 and 43% respectively of these sub-groups (total 49%).

There was very little difference between the picture presented by the official statistics and by the reclassified data.

Information about the 473 persons who had died was sought from Medical Officers of Health; they replied that no formal notification of tuberculosis had been received before death in 99 cases. These 99 deaths were examined, and it was found that 53 had been assigned to tuberculosis and 46 to other causes. Information from certifying doctors showed 51 as due to tuberculosis and 48 to other causes. The disease was considered to have been active in 59 and inactive in 40.

On the basis of these 99 cases it appeared that about 60% of the patients had been suffering from active tuberculosis at the time of death although they were not known to the tuberculosis service. Cases of tuberculosis coming to notice of Medical Officers of Health only after death comprise about one-quarter of the total number of deaths assigned to tuberculosis.

H. G. Calwell

CARTWRIGHT, Ann, MARTIN, F. M. & THOMSON, J. G. **Community Aspects of a Mass Radiography Campaign.** *Med. Officer.* 1959, June 5, v. 101, No. 23, 313–17.

A mass radiography campaign was carried out in Edinburgh in 1958, and in connection with it the authors carried out 2 interview surveys, one before and the other after the campaign. They have already published some of their general findings on public beliefs and opinions concerning tuberculosis as discovered in the surveys [this *Bulletin*, 1958, v. 33, 448]. The total number of completed interviews before the campaign was 554 and after it 498. Some 78% of the persons in the sample had been X-rayed, which was a higher proportion than among people who were not interviewed.

In the pre-campaign enquiry it had been found that the proportion of interviewed persons who said they intended to be X-rayed declined with increasing age but in the event the proportion of those who attended at the mass radiography units varied little with age. This was most probably due to the special inducements offered the elderly to attend and to the amount of propaganda directed at them.

The pre-campaign survey also indicated that there was a likelihood of a smaller proportion of professional than of manual or clerical workers attending for examination but in fact the proportion X-rayed did not vary significantly between occupational classes.

It was possible to compare the expressed intention of those interviewed with their action. The proportion of persons who expressed an intention to be X-rayed but who failed to attend varied from 6% of those in professional or intermediate occupations to 21% of unskilled manual workers. 10% of those in the professional or similar group said they would not attend but did so, and 12% who were uncertain at the time of interview finally attended. About 5% of the entire sample, who neither intended to be nor were X-rayed showed no significant variation in the proportionate size of different occupational groups included.

No greater knowledge of the causes or effects of tuberculosis was found in those who came to be X-rayed than in those who did not do so. It was found, however, that those who were not X-rayed were more likely to have said that if they had the disease they would prefer not to know and less likely to hold the opinion that it was important for people of their age to be X-rayed.

The reasons given for not attending were examined. Only 16% of the 61 persons concerned raised any positive objection to X-ray examination or the campaign. The main reasons were inconvenience (12), illness (16) and having been X-rayed recently (8). More than three-quarters of all those X-rayed came from households in which all other eligible members had also responded. This shows the influence of the family group and of publicity directed to and through it.

Newspapers, magazines, household visitors, posters and loudspeaker vans were the most effective means of advertisement; radio and television affected only one-third and films only 12%. The proportion of persons spontaneously recalling different forms of publicity did not vary markedly between those who did and did not attend. There was evidence that the level of public information about tuberculosis had been slightly but significantly raised by the campaign. *H. G. Calwell*

WARAWDEKAR, M. S. & SHAH, J. R. **Pulmonary Tuberculosis in the Contacts. A Mass Miniature Roentgenographic Study.** *Indian J. Med. Sci.* 1958, Oct., v. 12, No. 10, 797–801.

The authors set out to ascertain the value of submitting to mass miniature X-ray examination all the family contacts of newly diagnosed patients at a clinic in Bombay. This was done in the years 1951, 1952, 1954 and 1957.

There were 7,305 contacts of 1,605 patients. Of these 514 were said to be positive for thoracic tuberculosis. A classification into age, sex, and type of disease is given. As regards the type of disease, the relatively large number (56) of enlarged unhealed glands is interesting. 7% of contacts had pulmonary tuberculosis, and 5·7% had disease requiring treatment. This does not tell the whole story as undoubtedly further cases would be found in a follow-up of the contacts found to be normal at the original examination. *F. H. Young*

POPP, L. Der Tb-Coombstest. **[The Tuberculosis Coombs-Test]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, June, v. 117, No. 6, 419–49, 4 figs. [19 refs.]

The English summary appended to the paper is as follows:—

"620 serum samples were examined using the tuberculosis Coombs-test (anti-globulin test in connection with the haemagglutination reaction of Middlebrook and Dubos). One third of the samples was taken from patients of tuberculosis hospitals, two thirds were sent for differential diagnostic purposes. The clinical data of these patients were collected by questionaries after the tests were done. The results were evaluated by statistical analysis of the antibody levels. This evaluation showed that incomplete antibodies, only detectable by the Coombs-test, nearly always are present in sera of persons with active tuberculosis. Complete antibodies are present less frequently. When tuberculous processes get more and more inactive the antibody production decreases and the fraction of sera containing complete antibodies increases.

"The serologic possibilities in the diagnosis of tuberculosis are evaluated by comparing the results of the tuberculosis Coombs-test, the hemolysis reaction of Middlebrook and the complement-fixation test with antigen "Essen". The author is of the opinion that the serology of immune antibodies elicited by blood cell antigens and the serology of tuberculosis show good correlation, as far as indirect hemagglutination tests are used.

"The methods used and the technical possibilities to avoid unspecific reactions are discussed."

FLANAGAN, P. & HENSLER, N. M. **The Course of Active Tuberculosis complicated by Pregnancy.** *J. Amer. Med. Ass.* 1959, June 13, v. 170, No. 7, 783–7, 3 figs. [14 refs.]

"In a series of 22 pregnant patients with active tuberculosis compared to 40 nonpregnant patients with comparable background data, there was no statistical difference in rate of bacteriological conversion, roentgenographic stabilization, or cavity closure. All but one of each group were original treatment cases.

"The results indicate that pregnancy does not alter the tuberculosis prognosis, provided the disease is treated the same as that disease not complicated by pregnancy."

FROSTAD, S. **Segmental Atelectasis in Children with Primary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 597–605, 2 figs. [27 refs.]

This paper from the Grefsen Sanatorium, Norway, discusses the findings in 90 children who had segmental atelectasis associated with primary tuberculosis. Bronchoscopy was performed on all, on some on many occasions. In 61 children (67·8%) lymph node compression, and in 25 (27·8%) lymph node perforation were found. A full table of all findings is given. In 32 children tubercle bacilli were isolated. In 28 children shadows suggesting cavitation were seen on X-ray films. A table giving the site of atelectasis is given.

Lymph node perforations occurred within 6 months of primary infection in 11 patients, and a further 9 within 12 months. One child had 2 perforations, 1 month and 11 respectively after the primary infection—the very early date of the first is difficult to understand. The latest was 33 months after primary infection. Symptoms produced were slight. Cough was present in only 7 out of 25, and abnormal bronchial sounds in 3. In no child was a satisfactory gain in weight noted. Antimicrobial treatment seemed to have little effect on perforation. 8 children perforated after 6–14 months' treatment.

Bronchograms were performed on 33 children at the end of treatment, and positive findings were noted in 27, bronchiectasis in 12, and bronchostenosis in 16. 31 segments were removed from 15 children. 12 of these children had progressive tuberculosis. 2 children developed meningitis. In 3 children only did extrapulmonary complications develop, but the time of

observation was too short to make sure that this was the sum total.

The author concludes that therapy at present is unsatisfactory. This is a good paper and should be read *in extenso*. *F. H. Young*

COOPER, W. **Pancytopenia associated with Disseminated Tuberculosis.** *Ann. Intern. Med.* 1959, June, v. 50, No. 6, 1497–501. [16 refs.]

SMITH, J. **How Chronic is Pulmonary Tuberculosis in the Elderly?** *Brit. Med. J.* 1959, June 6, 1448–51. [10 refs.]

The increased incidence of pulmonary tuberculosis in the elderly indicates the need for a fresh assessment of this type of disease. It used to be taught that in the elderly the disease was very chronic, but this paper throws doubt on this.

In 100 consecutive cases of newly diagnosed pulmonary tuberculosis in patients over 55, efforts were made to obtain previous chest films. 50 patients had had previous X-ray examinations. In 23 the chest was reported as clear, in 27 an abnormality was noted, and in 1 additional case a shoulder X-ray film had revealed early tuberculosis and 6 years later at 69 years there was gross cavitated disease.

The 23 films were reassessed and slight apical fibrosis noted in 2 cases; 2 calcified foci were noted in the apex of another. In the 27 there was inactive tuberculosis in 12, and evidence of tuberculosis was diagnosed retrospectively in 3. 47 patients were over 50 when the early films were taken. Only 12 of the 50 had been examined by X-ray more than 5 years before diagnosis (6 with clear films).

In 2 patients the tuberculosis had an onset resembling a primary focus. 3 patients appeared to have developed the disease by contact with a member of the family.

The conclusion is drawn that a single clear X-ray examination in the elderly is insufficient evidence that tuberculosis is unlikely to develop subsequently.

In the Glasgow mass X-ray drive less than two-thirds of the elderly could be persuaded to attend, so repeated mass X-ray is therefore impracticable.

Reliance must be placed on the realization among general practitioners of the likelihood of the occurrence of pulmonary tuberculosis in the elderly and the need for chest X-ray examinations in all suggestive cases.

This is a very useful contribution. *F. H. Young*

MORTON, J. W. & KHAN, I. **A Practical Routine for the Presurgical Evaluation of Lung Function in Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 474–83. [18 refs.]

The assessment of the lung function on patients who are candidates for resection in the treatment of pulmonary tuberculosis is important for 2 reasons: (1) whether after recovering from the operation the patient will be a respiratory cripple; (2) whether the patient's respiratory function is good enough to carry him through the critical few days following the operation. The first can be fairly accurately assessed from function tests, but the second requires more margin, and in critical cases may also depend on the degree of toxaemia produced by the operation, the courage of the patient, and the avoidance of complications.

This paper reports the results of pre-operative tests on 417 patients proposed for surgery in 1956 and 1957 at Willow Chest Hospital at Vancouver. Details of the investigation undertaken are given in full in tables, but in most cases the percentages of the predicted values of the maximum breathing capacity and the vital capacity were found to give most information. 92 of the 322 patients on whom operation was performed had the tests repeated 6 months after operation. Patients were divided into groups according to the size of the resection proposed.

Where the maximal breathing capacity was greater than 80% of the predicted value no patients were refused for lung dysfunction for unilateral or bilateral surgery, and only 1 of the latter group has had postoperative respiratory insufficiency in spite of a fairly high ratio of complications. Where the maximum breathing capacity was less than 80% of that predicted (57 patients) full investigations detailed in a table were performed (in a few investigation had not been completed when it was decided not to operate for other reasons).

18 patients were refused on the basis of poor pulmonary function. Generally speaking below 40% the maximum breathing capacity/predicted capacity made surgery inadvisable. Residual lung function estimation was not very helpful. The emphysema-like state which occurs in these patients is reflected by the arterial blood gases, though this is seldom indispensable. Bronchospirometry was useful in 15% of patients in this group.

Resection of approximately 2 segments does not eventually lead to a reduction of maximum breathing capacity but larger resections produce 8–12% reduction. The patients with poorest function are most likely to have complications.

This paper should be read in its entirety. *F. H. Young*

SCHNITSER, M. S. & FAILIE, T. I. Expérience de traitement de la tuberculose pulmonaire suivant la méthode d'inhalation tracheale de la streptomycine. **[Treatment of Pulmonary Tuberculosis by Means of Tracheal Inhalation of Streptomycin]** *Problemy Tuberkuloza.* 1959, v. 37, No. 3, 49–52, 3 figs. [In Russian.]

The following is a translation of the authors' summary:—

Results are given of the use of the tracheal inhalation of streptomycin in the treatment of 20 patients suffering from cavitating tuberculosis and bronchial tuberculosis.

By means of a special inhaler 0·1 to 0·25 gm. of streptomycin in 2·5 ml. of saline were introduced every day for 20 to 25 minutes or 0·25 to 0·5 gm. of streptomycin in 2 ml. of saline were introduced intratracheally.

In all patients toxic manifestations diminished. The

temperature returned to normal and the erythrocyte sedimentation rate fell in 5 of 8 patients. Tubercle bacilli disappeared from the sputum in 9 of 17 patients. Cough ceased in 16 of 20. In one patient the cavity disappeared and in 2 others the cavities became very small. *H. J. O'D. Burke-Gaffney*

TURNER, P. P. **Simplification of the Ferric Chloride Test for P.A.S. in Urine.** [Memoranda.] *Brit. Med. J.* 1959, June 13, 1514.

The ferric chloride test for para-aminosalicylic acid (PAS) in urine described in this paper "was developed as a simple method for field work in a primitive country" but can also be used in any clinic. The patient is given a piece of white blotting-paper measuring about 1 × 4 in. and told to wet one end with his urine. When the paper is returned a single drop of 3% ferric chloride solution is dropped on to it. If PAS is present there is an immediate reaction of a ring varying in colour from an intense violet-black to violet, which develops around the spreading yellow spot of ferric chloride solution.

It is claimed that this test has certain advantages over the other ferric chloride tests which are in use. It "can be performed very rapidly, is easily read, and is sensitive enough for the practical purpose of determining whether or not the patient is adhering to the regime of P.A.S. prescribed for him". Concentrations of PAS as low as 25 mgm. per 100 ml. of urine could easily be detected. *M. E. Delafield*

LOW, E. **Relapse Rate in a Two- to Eleven-Year Follow-Up Study of Patients with Pulmonary Tuberculosis treated with and without Antimicrobials and discharged from 1946 through 1955.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 612–21, 1 fig. [29 refs.]

Although it is quite obvious that patients treated adequately with antimicrobial drugs do better than those who are not, satisfactory comparative studies are uncommon.

This paper reports on 838 patients who were discharged from Fort Qu'Appelle Sanatorium. Apart from drug treatment the groups seem comparable. There was a minimum follow-up of 2 years. It is generally held that about 70% of patients who will relapse do so within 2 years. 4 groups are considered. Of 425 patients who had no drug treatment the cumulative relapse rate was 31·5%, of whom 21·2% had relapsed by the fourth anniversary of discharge. Of 191 who had more than 6 weeks' but less than 6 months' therapy, largely streptomycin alone, 21·8% relapsed. 17·1% had relapsed by the fourth anniversary. Of the 65 who had streptomycin and PAS for 6 months or more, 12·5% had relapsed, and of the 157 who had 6 months' or more treatment with multiple drugs including isoniazid 8·8% had relapsed by the fourth anniversary.

Certain provisos suggest that the "less than 6 months" group were an unfavourable group, whereas the "streptomycin-PAS" group were rather a favourable group. The patients in the multiple drug therapy group had increasingly long courses of treatment in the latter years with diminution of relapse rate.

F. H. Young

MILLER, F. J. W. **Peripheral Tuberculous Lymphadenitis in Childhood.** *Postgraduate Med. J.* 1959, June, v. 35, No. 404, 348–53, 3 figs.

This paper presents the author's views on the origin and treatment of peripheral tuberculous lymphadenitis in children in the north of England.

In the British Isles the number of children seen with tuberculous lymphadenitis is steadily declining because of the control of both human and bovine tuberculosis.

In the past superficial tuberculous adenitis has usually been attributed to bovine infection but it is important to remember that in infants and young children contact with a tuberculous adult may be followed by tonsillar cervical adenitis. An example is given of the infection of twins during their first 6 weeks of life which resulted in tuberculous tonsillar and cervical adenitis in one and a primary pulmonary tuberculous complex in the other.

Another danger for infants and young children is a tuberculous milk supply from a herd containing an undiscovered tuberculous cow. An example is given in which 4 children were thus infected.

In a series of 163 children with confirmed tuberculous adenitis there was evidence in 80–90% that the glandular enlargement was part of the primary complex [this *Bulletin*, 1958, v. 33, 450]. The primary focus heals slowly but rarely causes trouble. The regional glands remain enlarged, and abscess formation is usual if the glands are not dealt with. In children who are not given chemotherapy, if abscesses occur, there is a risk of further abscesses. The glands also calcify; calcification is uncommon in the first year and appears more commonly in the second or third year [*ibid.*, 1956, v. 31, 381].

The child with peripheral tuberculous lymphadenitis undergoes the same risk of miliary or meningeal tuberculosis or haematogenous lesions as a child whose primary complex is in the lung or abdomen.

Tuberculous adenitis may occur within a few weeks of primary infection or when a calcified or partially calcified gland breaks down. This not uncommonly follows an intercurrent infection. The usual onset is slow with absence of pain, muscle spasm or loss of function which are characteristic of an acute pyococcal infection. Occasionally, however, the onset may be acute.

When tuberculous infection is the cause of the adenitis the child is always a tuberculin reactor and there may also be signs of hypersensitivity such as erythema nodosum or phylctenular conjunctivitis.

In the author's experience chemotherapy alone is not sufficient to prevent abscess formation. He gives isoniazid and PAS with the result that the children improve in health and well-being and then excises the whole gland and its immediate neighbours under cover of streptomycin and isoniazid. When the wound is healed PAS is resumed and streptomycin withdrawn. Chemotherapy is continued for at least a year. If the

gland has broken down curettage and expression may be necessary or enzyme irrigation to soften the caseous contents. *H. G. Calwell*

SPIESS, H. Wann setzt nach der BCG-Vakzination der Impfschutz ein? Ein experimenteller Beitrag. [**The Period required for the Establishment of Effective Immunity after Vaccination with BCG: An experimental Study**] *Deut. med. Woch.* 1959, May 22, v. 84, No. 21, 982–4 & 1015, 3 figs.

After vaccination with BCG there is an interval of time before tuberculin conversion occurs. It may, in rare cases, be as short as 3 weeks, it is oftener 6 weeks, but it is usually 3 months and exceptionally 4–5 months. The failure of tuberculin sensitivity to develop after successful vaccination is rare. In guineapigs vaccination with the dose used in man (0·05–0·1 mgm.) sensitivity is usually found in 4–6 weeks.

The interval between vaccination and the development of immunity is estimated to be 6 weeks, and it is therefore the recommended practice to break contact between the person vaccinated and a known source of tuberculous infection for 6 weeks after vaccination. The appearance of post-vaccinal tuberculin sensitivity is the indication that resistance to super-infection has developed.

The BCG skin test may be positive several days after vaccination and before the appearance of tuberculin sensitivity, and the question is asked whether the protective effect of vaccination is present during this early stage or only after the development of tuberculin sensitivity. The author has investigated this experimentally.

60 guineapigs were divided into 3 groups and vaccinated with 0·1 mgm. of dried BCG. 9, 20 and 39 days later they were inoculated subcutaneously with 10^{-3} mgm. of a virulent tubercle bacillus (Tb 49). 10 unvaccinated animals were similarly infected as controls. The period of survival of all groups and the extent of the tuberculosis found in lungs, liver, spleen and lymph nodes were examined.

The guineapigs infected 9 days after vaccination had the same amount of disease as the control animals. Those infected at 20 days showed no clear evidence of immunity but 14 of the 18 animals infected at 39 days survived for 8 months and showed much less disease than any of the other groups.

As a result of their low natural resistance to tuberculous infection the vaccinated guineapigs were protected against superinfection only in that the extent of the tuberculous lesions which developed was curtailed. The extent of such curtailment is shown by the finding that the average weight of the spleen in the animals vaccinated at 39 days was about one-half that in the other groups.

It is concluded that the occurrence of post-vaccinal tuberculin conversion indicates the onset of effective immunity (although they are not related in degree) and that the clinical practice of avoiding exposure to tuberculous infection for at least 6 weeks after vaccination is supported by the above experimental findings.

H. G. Calwell

VENEREAL DISEASES

MERRIWEATHER, A. M. **Endemic Syphilis - "Dichuchwa" - in the Bechuanaland Protectorate.** *Central African J. of Med.* 1959, Apr., v. 5, No. 4, 181–5, 8 pls. [11 refs.]

The endemic syphilis referred to here is probably the same as bejel, njovera and the endemic syphilis of Bosnia. Among the Bakwena it is known as dichuchwa and its incidence in this tribe varies from 37% up to 72% in one village. Out of 35,043 persons examined 9,656 were found positive including 2 primary, 287 secondary, 205 tertiary and 9,162 latent. Primary lesions are rare and usually occur on the nipple of a mother nursing an infected child; most cases occur in children under 15 (80%); the common lesions are periostitis, mucous patches and condylomata lata. The early lesions tend to disappear after a few weeks or months and the disease then becomes latent; in a few cases late lesions develop including skin ulceration, gummata, nasopharyngeal ulceration and bone affections; cardiovascular lesions are rare and though the cerebrospinal fluid occasionally becomes positive tabes and GPI do not occur. Congenital syphilis is rare and this is explained by the fact that women pass into the latent stage before the child-bearing age [but is this the only explanation?].

Treatment with PAM is very effective and a mass treatment campaign combined with raising the living standards of the people is proving very successful.

8 beautifully produced plates show a primary sore, mucous patches, anal and axillary condylomata, gumma of the skin, nasopharyngeal ulceration, bone lesions and ganglia. *T. E. Osmond*

PORTNOY, J. **Complement-Fixation with Small Volumes of Reagents. Application to a *Treponema Pallidum* Complement-Fixation Test for Syphilis (TPCF 50).** *Amer. J. Clin. Path.* 1959, Apr., v. 31, No. 4, 316–22. [14 refs.]

Owing to high cost of antigen a *Treponema pallidum* complement-fixation test (designated as tpcf50) was evolved with volumes 8 times smaller than in the usual test; incubation was carried out in the water bath at 37°C. only and haemolysis calculated according to a visual scale; the technique is set out in detail.

1,198 sera from patients with various types of syphilis, treated and untreated, yaws, pinta, leprosy, diseases other than syphilis, biological false positive reactors (proved and unproved) and normals were submitted to the following reactions: VDRL slide, TPI, RPCF, TPCF and tpcf50. The last named agreed closely with the others in all types of syphilis but was the most sensitive in treated early syphilis; it also agreed with the others in yaws and pinta but was much more reliable in leprosy than any of the others except TPI; it gave fewer positives than any except VDRL in diseases other than syphilis and the lowest figures in known biological false positive reactors; curiously enough in the case of presumed normal sera the tpcf50 gave 3·6% and TPCF 12·5% positive results compared with 0·3%, 1·5% and 0·9% with the other 3 tests.

It is concluded that the tpcf50 test is economical in antigen and can be completed in 1 day; it appears to be superior to the TPCF test and showed good agreement with the TPI test in the non-syphilitic group.

For details of technique the original should be consulted. *T. E. Osmond*

ITO, Y., FUKUI, T. & SHIROSHITA, T. **Hemolysis on Paper. IV. A Variation for Filter Paper Method and its Application.** *Acta Scholae Med. Univ. in Kioto.* 1959, v. 36, No. 1, 36–40, 6 figs. (5 on 2 pls.)

"A simple variation of the technique for detecting hemolysis using filter paper has been presented. The practical application of the method has been attempted in reading the results of several hemolytic reactions, and the usability and reproductability of the technique were found to be satisfying."

[See this *Bulletin*, 1958, v. 33, 944.]

LEVY, B. **The Treatment of Non-Gonococcal Urethritis with Spiramycin (Rovamycin).** *J. Roy. Army Med. Corps.* 1959, Apr., v. 105, No. 2, 87–9.

Spiramycin is active against the gonococcus and some viruses and is said to be useful in non-gonococcal urethritis (NGU); it has the advantage that it does not upset the normal intestinal flora.

This author treated 48 patients with NGU and apparently cured 38; these were mostly followed for 12 weeks but a few for shorter periods. Dosage was 5 gm. in 5 days or 7 gm. in 7 days; there was little difference in results; previous treatment did not appear to affect the issue.

The average incubation period was 27 days with extremes of 12 and 50 days. Side effects were negligible. *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases.

SARFATY, G. **Severe Tetanus treated with d-Tubocurarine Chloride ("Tubarine") and Tank Respiration.** *Med. J. Australia.* 1959, Apr. 11, v. 1, No. 15, 496–9, 1 fig. [18 refs.]

A boy of 14 suffering from severe tetanus was treated with tubocurarine, sedatives, and tracheotomy. Artificial ventilation was carried out by tank respirator and the authors regard this as preferable to the more usual positive-pressure method. [Full details of treatment are given; it is assumed too often that positive pressure ventilation must follow tracheotomy.]

A. B. Christie

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis. Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 169. **Joint WHO/FAO Expert Committee on Zoonoses. Second Report.** Stockholm. 11–16 August 1958. 83 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

The second report of the Expert Committee on Zoonoses re-defines the subject as "those diseases and infections which are naturally transmitted between vertebrate animals and man" and in an appendix gives a list, not comprehensive, but which includes the major examples of virus, rickettsial, bacterial, fungus, protozoal and helminth diseases; also "arthropod and insect" [*sic*] infestations, which incidentally come outside their own definition and clearly should not be regarded as zoonoses. There are numerous minor errors or omissions in this list [*e.g.* armadillos and opossums are not mentioned as reservoirs of Chagas's disease, the role of animals is omitted in malaria and filariasis], and the list itself could be usefully expanded to show primary and liaison animal hosts respectively.

In this report the following infections are particularly considered: salmonellosis, leptospirosis, anthrax, Q fever, arthropod-borne and listerian encephalitides, animal tuberculosis, psittacosis, hydatid disease, toxoplasmosis, larva migrans, ringworm, fascioliasis, schistosomiasis, tularaemia and cat-scratch disease. In reviewing these conditions, the Committee again goes beyond its subject and discusses matters such as the therapy and diagnosis of the diseases in man; such aspects could well be left for consideration by other bodies, but fortunately the relevant and strictly "zoonosis" side of the question also receives detailed consideration, particularly in the realm of epidemiology, the ecology of wild animal reservoirs, the treatment of meat or other animal products, as the connecting link (*e.g.* in salmonellosis, anthrax and Q fever), and control. There are 14 appendices, many of which contain useful and practical methods, and the whole report, in spite of irrelevancies, provides a good and up-to-date summary of the particular zoonoses considered.

P. C. C. Garnham

PANE, A. & MANZILLO, G. Rilievi statistici sul comportamento dell'infezione brucellare nel periodo 1948–1957. [**Brucellosis in the Period 1948–1957. Statistical Observations**] *Acta Med. Italica.* 1958, June, v. 13, No. 6, 144–51, 6 graphs. [10 refs.]

The figures given by the authors are collected from the "D. Cotugno" hospital at Naples and deal not

only with cases from Naples province but also from those round about. They only accept as positive those who were "Wright + 200" or had positive blood culture.

For the decennium the numbers per year varied from a maximum of 75 in 1951 to a minimum of 30 in 1957, and of the total of 467 cases 294 were male. The season of highest incidence was late spring early summer, and the age incidence was greatest in the 15–25 group with a peak at 20. There are a number of mathematical calculations but the authors suggest that their figures show (1) a slight diminution in the frequency of the malady; (2) the mainly seasonal character; (3) a sex and age incidence, males and the 15–30 age-group being chiefly affected. They do not consider, however, that the slight lessening in numbers is such as to permit prognostications of a rosy future.

[The standards selected are strict and it would have been interesting to have had figures of patients with low agglutination titres (*e.g.* 1 : 20 or so) where diagnosis is difficult. The type of organism is not mentioned (on the continent *Br. melitensis* is becoming increasingly frequent in cattle in certain countries).]

W. K. Dunscombe

AMANZHULOV, R. S. & REMENTSOVA, M. M. **Simultaneous Vaccination of Humans against Tularaemia and Brucellosis. I.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 177–81. [Translated from Russian.]

One of the authors vaccinated himself against tularaemia and brucellosis simultaneously using dry living vaccine subcutaneously for brucellosis and a similar vaccine intradermally for tularaemia, without ill effect. This encouraged the authors to use the same method for inoculation of a number of persons in a locality where cases of tularaemia and brucellosis were rife. The method used was injection of 1·0 ml. of dried living brucellosis vaccine subcutaneously on the left shoulder and living tularaemia vaccine intradermally on the right shoulder by rubbing it into 4 superficial scratches. The results showed that local and general reactions were more frequent when the vaccines were administered simultaneously by this method than when they were administered separately. In another series of experiments, however, both vaccines were administered intradermally through four superficial scratches simultaneously and fewer reactions were observed.

The advantage of simultaneous vaccination is saving of time. When vaccinating against tularaemia first and brucellosis afterwards an interval of 40 days is required; when vaccinating against brucellosis first and then against tularaemia the interval is 10 days. By simultaneous vaccination the population are safeguarded against both tularaemia and brucellosis in the shortest possible time in enzootic centres of infection.

Administration of both vaccines dermally results in fewer reactions, simplifies the problem of vaccination and eliminates the need to test beforehand those about to be vaccinated.

P. A. Clearkin

PARNAS, J. *et al.* Résultats des recherches d'ensemble des expéditions scientifiques des années 1954, 1955, 1956 et 1957 sur les leptospiroses. [**Results of Combined Investigations on Leptospirosis of Scientific Expeditions in the Years 1954, 1955, 1956 and 1957**] *Arch. Inst. Pasteur de Tunis.* 1958, Sept.–Dec., v. 35, Nos. 3/4, 275–300.

This article reports the results obtained in an investigation of the epidemiology of leptospirosis in an agricultural area near Lublin, Poland; some of the earlier work was described by PARNAS and DOMBROWSKI [this *Bulletin*, 1958, v. 33, 576]. As the aim was to elucidate the effects of a number of factors the team included workers trained in a variety of disciplines—zoology, entomology, chemistry, geology, meteorology, pathology, microbiology and general medicine. [It is impossible therefore to give more than an outline of the vast amount of data compressed into this article.]

The region studied was in undulating country with many small valleys and included agricultural land, marshes, swamps, wooded areas and numerous small lakes. Samples of soil and water, taken from numerous localities in the area, were found to vary from weakly acid to mildly alkaline in reaction and, with one exception, all the types of soil retained water well.

Large numbers of rodents and other small mammals were trapped and examined. Their ectoparasites were identified and counted, but none showed any evidence of leptospiral infection. Serological and cultural investigations indicated that *Arvicola terrestris, Microtus arvalis* and *M. ratticeps* were the chief carriers; *Leptospira grippotyphosa* was the predominant serotype present, followed by *L. sejroe.* In addition a few strains of *L. autumnalis, L. bataviae, L. icterohaemorrhagiae, L. poi* and *L. saxkoebing* were isolated.

Agglutinins, mainly for *L. grippotyphosa* or *L. sejroe,* were found in a high proportion of healthy domestic animals, and the same two serotypes were the common cause of the human cases of leptospirosis.

The inhabitants of the area were almost all peasants engaged in small-scale agriculture. Not only were they exposed to risk of infection in wet fields, but the level of general hygiene in their home surroundings was low. Water was generally obtained from shallow wells unprotected from risk of contamination by domestic or feral animals. Intensive efforts are being made to improve rural water supplies and to raise the general level of hygiene. Extensive land drainage schemes have also been approved to reduce the swampy nature of much of the agricultural land.

Prophylactic immunization with a killed vaccine composed of 4 parts of *L. grippotyphosa* to 1 of *L. sejroe* was begun in 1957. None of the vaccinated persons contracted leptospirosis, but it happened that very few cases occurred that year among the unvaccinated (as compared with 426 cases in 1955) so no estimation could be made of the efficacy of the vaccine.

J. C. Broom

POLLARD, M. **Recent Developments in the Epidemiology of Psittacosis.** *Texas Reports on Biol. & Med.* 1959, v. 17, No. 2, 186–93. [39 refs.]

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

ENGLISH, Mary P. & GIBSON, Mary D. **Studies in the Epidemiology of Tinea pedis. I. Tinea pedis in Schoolchildren.** *Brit. Med. J.* 1959, June 6, 1442–6, 2 figs. [14 refs.] **II. Dermatophytes on the Floors of Swimming-Baths.** *Ibid.* 1446–8.

These authors describe and discuss in part I the results of an intensive study of the epidemiology of tinea pedis in schoolchildren. Data are based on a survey of 1,839 boys and 2,061 girls between the ages of 11 and 14 years from 12 secondary modern schools, and 894 boys aged between 7 and 10 years in 4 junior schools, all situated in the Bristol area. The incidence of infection is considered in relation to a number of factors including: district, age, sex, degree of cleanliness, social status, presence or absence of non-mycotic lesions, use of school and district swimming-baths and footwear. The authors conclude from their results that tinea pedis is not rare before the age of puberty but that its incidence increases with age; that there is a higher rate of infection among boys than among girls, but that this may be explained in part by the greater use which boys make of the local swimming-baths in out-of-school periods; that there is no correlation between the incidence of infection and attendance at swimming classes in school as regards boys, and that as regards girls, infection is significantly higher among non-bathers; that social status and degree of cleanliness do not influence incidence of infection; that the presence of non-mycotic lesions does not appear to predispose to infection to a significant degree; that footwear used at swimming-baths, since it is adequately sterilized, could not be taken into account; finally, that on the whole the main factor influencing incidence of infection appears to be a geographical one, in so far as boys are concerned, and could be accounted for by the frequency of the use of the local swimming-bath by schools in the district and by boys during out-of-school periods. Of 179 infections, 84% were caused by *Trichophyton mentagrophytes*, 7·2% by *T. rubrum*, 3·9% by *Epidermophyton floccosum*, and 4·4% were considered as being positive only on the basis of microscopical examination.

In part II these authors describe and discuss the results of their investigations into the occurrence of dermatophytes on the floors of public swimming-baths frequented by schoolchildren in the Bristol area. Using the methods devised by GENTLES [this *Bulletin*, 1957, v. 32, 149] they found that a relatively large number of sampling pads were contaminated by dermatophytes, but that these were all of the same species, namely, *T. mentagrophytes*. However, samplings from the feet of swimming-bath staff revealed all 3 species of dermatophytes causing tinea pedis, namely, *T. mentagrophytes*, *T. rubrum* and *E. floccosum*. A higher number of positive samples obtained from the floors of the boys' accommodation than from the floors of the girls' accommodation, as well as a higher incidence of infection among swimming-bath attendants who used the baths than among those who did not use them provided strong confirmation of the main conclusion reached in part I of these investigations, that the local swimming-bath is an important source of infection with tinea pedis. However, in mitigation of this conclusion is the fact that adequate brushing down and sluicing are reasonably effective methods of removing infected particles. *C. J. La Touche*

PARDO-CASTELLO, V., TRESPALACIOS, F., FARIÑAS, P. & FERNÁNDEZ BAQUERO, G. El tratamiento de las micosis superficiales de la piel con griseofulvin. **[The Treatment of Superficial Mycoses of the Skin with Griseofulvin]** *Bol. Soc. Cubana de Dermat. y Sifil.* 1959, Mar., v. 16, No. 1, 1–11.

The English summary appended to the paper is as follows:—

"1.—From work carried out by us in 1957 and 1958 it may be concluded that griseofulvin has no parasiticidal action when used locally as a cream, ointment, alcoholic solution or in powder form in various proportions.

"2.—Griseofulvin administered by mouth in the form of tablets containing 250 mg. of the drug. in doses of 500 to 2,000 mg. daily is markedly effective on the superficial mycoses affecting the skin, hair and nails. It seems ineffective in deep mycoses.

"3.—In two cases of chromoblastomycosis and in one case of cryptococcosis, griseofulvin administered by the oral route proved ineffective. New attempts at the treatment of deep mycoses might be suggested, using the drug by parenteral injection. Animal experiments must be carried out first to investigate the toxicity of this drug by that route.

"4—Griseofulvin is now the treatment of choice, administered by oral route, in all cases of superficial mycoses.

"5.—In two patients, symptoms of intolerance were observed, such as headache, abdominal cramps and nausea following the first few doses of griseofulvin. After the suppression of the drug, no further symptoms were observed and no changes in the blood could be detected. No renal complications have been observed. In all other patients tolerance was good.

"6.—Of 37 patients treated, 13 were cases of eczema marginatum, 2 of pityriasis versicolor, 6 of tinea capitis, 4 of onychomycoses, 9 of dermatophytosis of the feet, 2 of chromoblastomycosis and one of cutaneous cryptococcosis. The drug was effective in curing all superficial lesions of the skin and hair

in a period of two to three weeks, although medication was continued for two weeks longer. In cases affecting the nails; from two to four months may be necessary before treatment is completely successful.

"7.—Griseofulvin seems to act as a parasitostatic in superficial mycoses. It has been reported that if hairs from tinea patients under this treatment or scales from cutaneous lesions are washed and planted in Sabouraud's medium, the fungus may grow after griseofulvin has been eliminated."

McLean, W. C. & Fitz-Hugh, G. S. **Blastomycosis as encountered in the Practice of Otolaryngology.** *Southern Med. J.* 1959, June, v. 52, No. 6, 667–72, 2 figs. [15 refs.] Discussion 672–3.

A review and account of 2 cases.

Christie, A. **The Disease Spectrum of Human Histoplasmosis.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 544–55, 1 fig. [16 refs.]

In the John Phillips Memorial lecture the author gives an up-to-date account of human histoplasmosis, especially the benign form. In the United States of America the main area of endemicity is a pear-shaped one bounded by St. Louis, Missouri, and Little Rock, Arkansas, with northern Georgia and Columbus, Ohio, in the middle.

The histoplasmin test has many resemblances to the tuberculin reaction, but massive progressive infection may produce a negative reaction. Clinically the disease is often like tuberculosis. The progressive disseminated type has cutaneous or mucocutaneous lesions in 50% of cases. In children it resembles aleukaemic leukaemia. This type is usually fatal. In the benign variety many cases are symptomless, but usually there is splenomegaly, ulceration of the pharynx, adenopathy and pulmonary infiltration. The fungus can usually be found in the lesions. The histoplasmin tests and demonstration of the fungi are the sheet anchors in diagnosis. The complement-fixation test is useful in the acute stages.

Treatment is discussed and sulphonamides are recommended. 5 cases have been treated with these drugs sufficient to produce a plasma level of 12–15 mgm.% with success.

This is a useful and authoritative paper.

F. H. Young

Yamato, H., Hitomi, H., Maekawa, S., Mimura, K., Hamazaki, Y., Ogawa, K. & Uejima, A. **A Case of Histoplasmosis. Report 1. Clinical, Mycological and Pathological Observations.** *Acta Med. Okayama.* 1957, Dec., v. 11, No. 4, 347–64, 20 figs. (19 on 4 pls.) [30 refs.]

"In our country it has been believed that there is no histoplasmosis here in Japan. However, from the above clinical signs, radiological characteristics, laboratory tests, pathological and mycological examinations, and experimental findings, we believe this is the first case of histoplasmosis in Japan."

Ann. Intern. Med. 1958, Sept., v. 49, No. 3, 642–61, 10 figs. **Cryptococcosis: Clinical Staff Conference at the National Institutes of Health** [McCullough, N. B. (Moderator); Louria, D. B., Hilbish, T. F., Thomas, L. B. & Emmons, C. (Discussants).]

This is a discussion on the clinical and pathological features of cryptococcosis based on 10 cases. The discussion was started by a clinical description of 4 cases with relevant X-ray pictures. In 1 the picture was that of generalized disease without abnormalities of the central nervous system; in the other 3 central nervous system features predominated.

McCullough said that the occurrence of cryptococcosis was underestimated. The occurrence of pulmonary cryptococcosis without disease elsewhere, and the presence of pulmonary lesions in cases of meningitis suggest that the lungs are the portal of entry. Often the picture suggests tuberculosis and the diagnosis always depends on the isolation of the organism from sputum or material obtained surgically. The onset may be acute or insidious. A valuable account of the clinical picture of the 2 types follows.

In the meningeal type the picture is not diagnostic. Difficulties arise because the central nervous system may be normal. The organisms may be recovered by injection of material into mice.

Thomas dealt with the pathology as found in 7 cases (2 of these were described above). He pointed out that cryptococcosis is often a terminal infection in patients suffering from other chronic diseases, *e.g.* sarcoidosis, rheumatic heart disease or neoplasms. The subarachnoid space is often filled with polymorphonuclear lymphocytic and eosinophil cells. Circumscribed lesions containing cryptococci are found in the brain substance. In the lungs, abscesses of a similar character are found widely scattered throughout.

In haematoxylin-stained sections the organism is spherical and has a clear halo. Emmons, a mycologist, described the capsule in detail. The organism is not contagious and leads a saprophytic existence, and can be found in pigeon nests.

Louria reported that treatment had been disappointing. Sulphonamides are reported to have been useful in some cases. *In vitro* amphotericin B is fungistatic and gives good results in mice. 6 patients were treated with oral amphotericin in doses up to 5 gm. daily; good results were reported in cases of disseminated disease, but it was ineffective in dealing with central nervous system involvement.

Careful study of this discussion will be very valuable to those interested in cryptococcal disease.

F. H. Young

Nevill, L. M. B. & Cooke, E. R. N. **Human Cryptococcosis in Kenya.** *East African Med. J.* 1959, Apr., v. 36, No. 4, 209–19, 3 figs. [15 refs.]

"The history and pathology of human cryptococcosis are reviewed and seven cases described, six cases presenting with meningitis and one with epilepsy. Two of our cases had obvious lung lesions.

"The bacteriology and epidemiology are discussed

and the association between the disease and women working on the land noted."

Cycloheximide 15 mgm. in 1·5 ml. by intravenous injection, was given daily to 2 patients for 2 and 3 months respectively, together with polymyxin 50,000 units intrathecally each day for the first few days. The response to this treatment was encouraging and both patients were ultimately discharged from hospital.

Peter Abbott

FRISK, Å. & HOLMGREN, B. Amphotericin B vid Cryptococcusmeningit. [**Amphotericin B in Cryptococcal Meningitis**] *Nordisk Med.* 1959, June 18, v. 61, No. 25, 927–9, 1 fig. [12 refs.]

The English summary appended to the paper is as follows:—

"A brief review of the clinical symptoms in cryptococcosis is presented, followed by a report on a case of cryptococcal meningitis in a 55 year old man, successfully treated with amphotericin B (fungizone, Squibb). The patient was given 34 intravenous infusions during 55 days with rising doses up to 75 mg daily. He received a total of 1.86 g of the drug. Initially he developed moderate toxic manifestations, as headache, vomiting, chills, fever, and a rise in non-protein nitrogen. After administration of antipyretics and antihistamines, however, these reactions diminished. The patient showed rapid clinical improvement. Seven months after the end of treatment he returned to normal activities without any subjective or objective signs or symptoms. Serial examinations of cerebrospinal fluid showed a marked improvement in cell counts and chemistry, with quite normal values on the last two occasions.

"The result of the treatment indicates that in all probability, amphotericin B completely cured this patient of his cryptococcal meningitis."

FITZPATRICK, M. J., RUBIN, H. & POSER, C. M. **The Treatment of Cryptococcal Meningitis with Amphotericin B, a New Fungicidal Agent.** *Ann. Intern. Med.* 1958, Aug., v. 49, No. 2, 249–59. [14 refs.]

Case histories of 3 patients suffering from cryptococcal (torular) meningitis are given: meningitic symptoms lasted for 2 months, 7 months and 11 years: cerebrospinal fluid findings are given in detail and the similarity to findings in tuberculous meningitis, including lower sugar, is stressed. Amphotericin B was given orally to the first patient without effect. The second patient was treated by slow intravenous infusion of the drug with apparent cure. The third patient had intravenous and later intrathecal therapy: this latter produced a marked reaction resembling that following the intrathecal injection of tuberculin, and was followed by clinical improvement, though not cure. [The article is well worth reading in full for its description of this rare form of meningitis.] *A. B. Christie*

SMITH, H. W. & YANAGISAWA, E. **Rhinomucormycosis. Report of a Fatal Case.** *New England J. of Med.* 1959, May 14, v. 260, No. 20, 1007–12, 7 figs. [33 refs.]

After a brief introduction in which the history, aetiology and pathology of the disease are outlined and details of 22 cases from the literature are tabulated, the authors describe a fatal case in a Negro with a long past history of diabetes but with a recent history of only 2 days' duration which began with the gradual onset of "dull, steady, nonradiating pain to the right frontal region of the head". On admission, the right eye was bulging forward conspicuously and was completely closed.

After a mass consisting of dried bloody discharge had been removed from the nose, it was seen that the middle and inferior turbinates on the right side were grey-black in colour, a feature said to be characteristic of this disease. Sections from biopsies taken from these structures and from the ethmoid-sinus mucosa at operation revealed "large, branching, non-septate hyphae". A conspicuous growth of fungus was also observed at autopsy in the operative site. In necropsy material hyphae were found in sections from a number of sites besides the nasal cavity, namely, meninges, brain, dural sinuses and major cerebral arteries, as well as in the tissues of the right orbit.

[It is to be regretted that the aetiological agent, *Rhizopus arrhizus*, is not more fully described and that its appearance in the tissues is not more clearly illustrated in this otherwise most interesting report.]

C. P. La Touche

Rheumatic Diseases

FEINSTEIN, A. R. & DI MASSA, R. **Prognostic Significance of Valvular Involvement in Acute Rheumatic Fever.** *New England J. of Med.* 1959, May 14, v. 260, No. 20, 1001–7. [26 refs.]

359 patients receiving antimicrobial prophylaxis against streptococcal infection after an attack of acute rheumatism were kept under observation for periods ranging from 2 to 9 years. The findings during this surveillance were compared with findings during the acute attack and it was concluded that in the acute attack auscultatory findings were of primary importance in predicting cardiac prognosis. Definite evidence of cardiac enlargement, congestive heart failure and pericarditis occurred almost exclusively in patients who had auscultatory signs of valvulitis. The diagnosis of "valvulitis"

was made in patients who developed diastolic murmurs during the attack; when there was a local apical murmur radiating to the axilla or a doubtful diastolic murmur the diagnosis of "probable valvulitis" was made. "No valvulitis" was the diagnosis when these auscultatory signs were absent although other signs such as prolonged PR intervals or cardiac enlargement might be present. Of the "valvulitis" group 67% developed rheumatic heart disease, of the "probable valvulitis" group 25%, of the "no valvulitis" group none. *A. B. Christie*

MILLER, J. M. **Prophylaxis of Rheumatic Fever and Rheumatic Heart Disease.** *New England J. of Med.* 1959, Jan. 29, v. 260, No. 5, 220–30. [131 refs.]

This is a well-documented review (131 references) of the aetiology of rheumatic fever *qua* streptococcal infection, clinical and sub-clinical, and of the prevention of rheumatic heart disease by chemoprophylaxis against streptococcal infections over a long period of years. There is nothing new in the article, but it is a good summary of the subject.

Adequate and early penicillin treatment of acute streptococcal infections not only removes the causative organisms but helps to stop the anti-streptolysin titre from rising to a dangerous extent, and correspondingly reduces the tendency to rheumatic complications. Persons who have had an attack of rheumatic fever, or who have damaged heart valves, should have penicillin prophylaxis regularly by monthly injections or by tablets daily by mouth during the whole vulnerable period of life—which may be up to age 40 or longer. Where there is any evidence of penicillin sensitivity, sulphonamides are recommended in the form of 0·5 gm. sulphadiazine twice daily. [There is no reference to the new slowly excreted sulphonamides, by means of which the drug-taking may be reduced to once or twice a week, or to the question whether the sulphonamide-resistant streptococci, reported in great numbers in 1945 and 1946, are present to a significant extent today. A re-appraisal of sulphonamides in the prophylaxis of streptococcal infections seems overdue in view of the increasing allergy to penicillin.] *H. Stanley Banks*

KOHLER, W. Die Serologie des Rheumatismus und der Streptokokkeninfectionen. [**The Serology of Rheumatism and Streptococcal Infection.**]

This book is reviewed on p. 965.

Cancer

REGISTRAR GENERAL. **The Registrar General's Statistical Review of England and Wales for the Year 1953. Supplement on Cancer.** pp. ix + 105, 8 diagrams. 1958. London: H.M. Stationery Office. [7s. 6d.]

This volume adds to the information given on the National Cancer Registration Scheme in the Supplement for 1952 by dealing specifically with 8 sites, corpus uteri and ovary in women, testis and penis in men, and in both sexes lip, tongue, mouth and pharynx, and oesophagus. New registrations in the years 1945–51, and the 5-year survival rates of those registered in the first 4 years of this period, are tabulated in detail by age, clinical stage, duration of symptomatic history and treatment. The mean age of patients with cancer of the corpus uteri registered was 60 years, and in 59·2% the growth was *early*, *i.e.* without invasion of adjoining tissue. Registrations were rare below 35 years of age and reached a peak at 55–59 years, though the death-rate rose steadily with age. Length of symptomatic history, averaging 7–8 months, had little effect on the clinical stage. Surgery alone or with radiotherapy was the more frequent mode of treatment, particularly in younger patients, but 46% of late cases had radiotherapy alone. The corrected 5-year survival rate, allowing for mortality from other causes, was 49% for all cases, varying from 67% for early to 46% for late cases treated radically. Corrected survival rates were appreciably less in older women, but were greater in those with longer symptomatic histories. A shorter duration of symptoms in early growths among older women suggested that the malignancy of the tumour increased with age.

Of the ovarian tumours only 22% were confined to the ovary itself. The mean age of registered patients was 54·5 years and the age distribution was similar to that for tumours of the corpus uteri. Mortality, however, did not increase steadily with age but flattened out at 55–59 years. The mean duration of symptoms for early and late cases was about 4½ months. Surgery was used in 95% of early and in 53% of late cases. The corrected 5-year survival rate was only 17% for all cases, but was 57% in early cases treated radically.

Registrations of cancer of the testis had a low mean age of 40·3 years, and the peak occurred at 35–39 years. The growth was localized in more than one-half, and metastatic spread was commoner in younger patients. Symptoms were present for an average of 4·9 months. Radical surgery with radiotherapy was used in 80% of early cases, and surgery alone in 17%. The corrected 5-year survival rate was 52%, with a maximum of 74% in early cases.

Patients registered with cancer of the penis averaged 64·5 years, and both registration and mortality increased steeply with age. The growth was confined to the penis

in 43%, this proportion being unaffected by length of history, which averaged 6 months. Surgery was the common form of treatment, though 28% of early cases received radiotherapy alone. The corrected 5-year survival rate was 55%.

Cancer of the lip was registered over 10 times as frequently in men as in women, but the course of the disease appeared to be similar in both sexes. Mean age at registration was about 66 years, both registration and mortality increasing steeply with age; 80% of cases were at the early primary stage, and the mean duration of symptoms was 6 months. Radiotherapy alone was employed in over four-fifths of early cases and the 5-year survival rate for all cases was high at 78%. Age had little influence on survival rates.

Cancer of the tongue was registered 3 times more frequently in men than in women, and both registration and mortality increased with age. In men only one-third of the growths were localized, but in women the proportion was over 50%. Mean duration of symptoms was, however, longer in women, 4·5 months compared with 3·7 for men. Radiotherapy alone was the treatment of choice in 70% of early cases, and surgery alone was employed in only 8%. 5-year survival rates were higher in women, 38% compared with 22% in men. In early cases the corresponding female and male rates were 57 and 47%. In both sexes the survival rate was high where the duration of symptoms was over 12 months.

The pattern with cancer of the mouth, pharynx and tonsil was also different in men and women. Registrations were over twice as common in men, and occurred later, the mean age being 66 years compared with 60 in women. Early cases were only 26% of male registrations, but 34% of female, these proportions falling with increasing age. The duration of symptoms was, however, longer in women, for early cases 8·8 months in women, 4·5 months in men. Radiotherapy alone was employed in 63% of early male cases, and in 47% of early female cases. The corrected survival rates for all cases were 23% for men but 32% for women, and for early cases 51 and 65%. For all stages of growth these rates were higher when the duration of symptoms exceeded 12 months.

Cancer of the oesophagus was also registered twice as frequently in men as in women. It was rare below 40 years, and the average age in both sexes was about 65 years. Early growths were a small proportion in both sexes, 15% in men and 19% in women, but metastatic spread was found in only 8%. Mean duration of symptoms was 4 months in men and nearly 5 months in women. Radical surgery was employed rather more often than radiotherapy alone in early cases, but overall as much as 39% were untreated. The survival rates were very low, 1·4% in men and 3·2% in women. Even for early cases offered radical treatment the rates were only 7 and 15%. *J. Knowelden*

STOCKS, P. **The Epidemiology of Cancer.** *Practitioner.* 1959, June, v. 182, 667–72. [12 refs.]

Laryngeal cancer shows pronounced epidemiological differences between the sexes. Among men the rates are greater in urban than in rural areas, they increase from professional to unskilled workers and they are high among makers and servers of alcoholic drinks. Among women mortality is greater in rural areas and no class gradient is evident. The distribution in the large towns of England and Wales is entirely different in the 2 sexes though the rates for each sex are correlated with those of oesophageal cancer. Cancer of the stomach shows some pronounced differences between countries. In England and Wales there is a significant correlation with atmospheric pollution after allowing for the density of population in the area. The high rates in parts of Wales show no connexion with dietary habits. There is evidence that constituents in the soil may play a part in causation.

Intestinal cancer appears to be less variable geographically. In Liverpool and the N. Wales area an association was found with the frequency of beer drinking but no correlation with the consumption of wine is evident in France. There appears to be some association between the incidence of rectal cancer and pipe smoking. Although the rate of mortality from carcinoma of the uterus rises according to the number of children a woman has borne, the factor responsible for the statistical relationship appears to be the commencement of frequent intercourse at an early age. A brief review of the evidence on lung cancer points to 2 causative agents—the smoking of cigarettes and atmospheric smoke. The validity of the evidence is reviewed and this leads to the conclusion that everything possible should be done to remove or prevent the production of carcinogens already known to be present, to educate people as to the risks and discourage boys and girls from acquiring the cigarette habit, and to reduce pollution of the air in towns by potentially carcinogenic substances. *A. Bradford Hill*

BERKSON, J. **The Statistical Investigation of Smoking and Cancer of the Lung.** *Proc. Staff Meetings Mayo Clinic.* 1959, Apr. 15, v. 34, No. 8, 206–25, 4 figs. [41 refs.]

The most definitive of the statistical investigations that have given rise to the theory that smoking causes cancer of the lung are the 2 prospective studies which have been carried out in England [this *Bulletin*, 1954, v. 29, 1059; 1957, v. 32, 145] and in the U.S.A. [*ibid.*, 1958, v. 33, 753, *bis*]. Some aspects of these studies are, however, open to serious criticism. For example, the first results reported from the American study showed death-rates that were low compared with the corresponding rates for the general population and the proportion of men recorded as smokers was unexpectedly small. Evidently the population studied was not representative of the reference population from which it was drawn and with such a selected sample spurious statistical associations could be produced. This objection was, however, weakened by the data recorded in a subsequent report, which showed that the death-rates had risen; moreover, had the association been spurious it would have been expected to decrease with the passage of time; whereas, if anything, it became stronger. A more important criticism is that the excess mortality among smokers is not confined to cancer of the lung, but in both the American and the British studies a clear association

with many other diseases is also demonstrated. And if, instead of presenting the data as proportional mortalities, they are presented to show the excess number of deaths among smokers (or heavy smokers) compared with non-smokers (or light smokers), it is found that cancer of the lung accounts for only a small proportion of the total. In other words, these studies prove too much and it may be doubted whether they can be regarded as providing any evidence for the existence of a specific lung cancer factor.

In the author's opinion it is desirable to seek a unified explanation for the general association observed, rather than to give one explanation for the association between smoking and cancer of the lung, another for that with vascular disease, and so on. 3 such explanations may be considered: (1) That the associations are spurious statistical phenomena arising perhaps from the unreliability of the basic data—the inaccuracies in the smoking histories and in the recorded causes of death; (2) that the association has a constitutional basis, that persons who are non-smokers or relatively light smokers are also disposed to longevity; (3) that smoking speeds up the normal process of aging.

The paper is concluded by 3 long notes in which the author develops his view that the use of mortality ratios to measure the effect of smoking is less appropriate than the measure of the actual numbers of excess deaths.

[The author's views on mortality ratios are interesting, but they do nothing to alter the fact that, relative to the position among non-smokers, the mortality among smokers is many times greater for lung cancer than for any other disease examined.] *Richard Doll*

HAMMOND, E. C. **Inhalation in relation to Type and Amount of Smoking.** *J. Amer. Statistical Ass.* 1959, Mar., v. 54, No. 285, 35–51, 1 fig.

A postal survey was made to obtain information on inhalation in relation to type and amount of smoking and the opportunity was taken to discover whether the form of the survey had any appreciable influence on the findings. It was found that a lower proportion of replies was received from an appeal which stressed an interest in cancer and smoking than when a reference to this interest was omitted and that a lower proportion was received when a business reply-paid envelope was enclosed than when a stamped addressed envelope. The source of the letter (American Cancer Society or Yale Statistical Laboratory) made little difference. The results with regard to the proportions of non-smokers and of different types of smokers were much the same, irrespective of any of the above factors and irrespective of whether the reply was received in response to the first letter or to a follow-up letter. Moreover, although only about 60–70% replied, the proportions of non-smokers in each age-group were similar to those obtained by the Bureau of the Census from a survey of a large random sample of the entire population. It is concluded that factors such as the wording of the covering letter had an effect on the percentage returns, but that they had little or no effect on the percentage distribution of the answers to questions on smoking habits.

Replies to the question on inhaling showed that the proportion of cigarette smokers who said that they inhaled (or that they inhaled deeply) increased with the amount of smoking between the 3 categories of men smoking less than one, about one, and over one packet a day, and the proportions decreased with increasing age under 40 years, to 40–59 years and to 60 years and over. The proportion of men who said they inhaled was much higher for cigarette smokers than for pipe and cigar smokers and higher for men who smoked only cigarettes than for men who smoked cigarettes and cigars. There was, however, little difference between the proportion of inhalers between those smoking plain cigarettes and filter tip cigarettes. The results agree with those reported by SCHWARTZ and DENOIX from France [this *Bulletin*, 1958, v. 33, 348]. It is suggested that they may account for the higher mortality for some diseases which has been recorded for cigarette smokers in comparison with pipe smokers, cigar smokers and mixed cigarette and cigar smokers. *Richard Doll*

See also p. 1020, BOHLIG, JACOB & KALLABIS [**Morbidity and Pathology of Lung Cancer with Asbestosis.**]

CAMPHYN, R. Les tumeurs pulmonaires primitives chez le Noir observées au service de pneumophtisiologie de Luluabourg. [**Primary Tumours of the Lung observed in Africans at the Chest Clinic in Luluabourg**] *Ann. Soc. Belge de Méd. Trop.* 1958, Aug. 31, v. 38, No. 4, 591–603, 4 figs. on 2 pls.

In a period of just over 2 years in 1955–7 the author and his colleagues diagnosed 19 primary intrathoracic tumours, 1 tracheal tumour and 3 laryngeal cancers in 1,933 patients treated at the centre, most of whom were suffering from pulmonary tuberculosis.

There were 17 epitheliomata, 1 oat-cell tumour and 1 adenocarcinoma in the intrathoracic group. Diagnosis was confirmed in 16 by bronchoscopy and histological examination (13) or at autopsy (3). Atelectasis was observed in 6 cases, massive pneumonitis with suppuration in 3, cavitation in 4, rounded apacities in 3, other appearances in 3.

These findings are described in considerable detail. *Charles Wilcocks*

MARNEFFE, J. Tumeurs malignes O.R.L. et maxillo-faciales au Ruanda-Urundi. [**Malignant Tumours of the Oto-rhino-laryngeal and Maxillofacial Areas in Ruanda-Urundi**] *Ann. Soc. Belge de Méd. Trop.* 1958, Aug. 31, v. 38, No. 4, 681–96, 9 figs. on pl. [11 refs.]

The problem of cancer is becoming more and more obtrusive in Africa as the great infective diseases are receding. In the Usumbura area the author's service has diagnosed 33 malignant or potentially malignant growths, by histological means, in the period 1956–8. These were included in the total of 86 benign or malignant growths discovered in 19,825 Africans.

25 of the growths were definitely malignant, comprising 13 epitheliomata, 2 adenocarcinomata (thyroid), 7 sarcomata, 2 Hodgkin's disease and 1 melanoma. The nasal fossae were involved in 6 of these, maxillae in 5, mandibles in 5, mouth in 2, thyroid in 2 and neck in 5. The patients were all adults, 14 were women and 11 men.

The author discusses the types of growths in some detail, and the possible aetiological factors which could have had a bearing on their formation. He points out that most patients were in an advanced state of disease when they first came for treatment, and that it is necessary to educate the public in this matter.

Charles Wilcocks

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

ANN. OCCUP. HYG. London. 1958, Dec., v. 1, No. 1, 1–133, numerous figs. [Numerous refs.] **Noise in Industry.**

[The *Annals of Occupational Hygiene* is a new international journal published for the British Occupational Hygiene Society by the Pergamon Press, with Dr. C. N. DAVIES as Editor in Chief. Papers presented at Conferences and Scientific Meetings of the British Occupational Hygiene Society will form the main contents of the Annals, but other contributions will be welcomed.]

This first issue is devoted to papers relating to *Noise in Industry*, which was the subject of the Society's 8th Conference, held in London on 1st April 1958. The subject is so well covered and documented that the issue will serve as an invaluable text book to all whose concern is the conservation of hearing in industry.

T. CAWTHORNE sets the scene in a paper entitled *The clinical and physiological effects of noise* (pp. 1–10) in which a review of the construction and function of the ear is followed by a graphic description of the pathological, clinical and social consequences of overstimulation of the ear by sound. The more nebulous, but nevertheless important, psychological effects of noise are discussed by A. CARPENTER (*The effects of noise on work*, pp. 42–54) who concludes that high noise levels in the region of 100 dB can interfere with those types of work in which continuous and monotonous attention is required.

T. S. LITTLER (*Noise measurement, analysis and evaluation of harmful effects*, pp. 11–27) reviews the basic physics of sound propagation, and of the measurement and analysis of noise. The nature of the excitation of the cochlea by applied sound is described, and this leads to a discussion of the relative merits of noise analysis by narrow band, critical band and octave band techniques. An important section of this paper is that in which the author proposes (in collaboration with Professor W. BURNS) a damage risk criterion, which is appreciably more stringent than current American standards. Data are given to show the degree of protection which may be expected from insert ear plugs and external muffs.

Principles of noise suppression by N. FLEMING and W. C. COPELAND (pp. 28–41) begins with the warning that many industrial processes are inherently and unavoidably noisy, and that in such cases careful planning is necessary in order to limit the spread of the noise. Much noise is avoidable, however, and minor changes in materials handling methods can produce substantial reductions in noise. The degree of sound reduction provided by insulating panels is largely a function of the superficial weight of the panel, and is greater at higher frequencies than at lower frequencies. At high frequencies the nature of the construction of the panel becomes more important. Insulating enclosures should be provided with sound-absorbing treatment on the inner surfaces. The uses of antivibration mountings, sound-attenuating ducts and silencers for low-frequency pulsations are also outlined.

R. HINCHCLIFFE poses the question *Has your worker a noise problem?* (pp. 55–67), and considers that a problem may arise from deleterious effects due to (a) interference with communications, (b) undue loudness, (c) annoyance, (d) influence on behaviour, (e) impairment of hearing, (f) physiological effects, and (g) increase of accident rate. The ways in which octave band analyses may be used to assess the degree of interference with speech communication are described. While supporting the damage risk criterion of Burns and Littler, the author points out that there is evidence in favour of the use of an energy-duration concept in assessing whether a noise exposure is hazardous or not. Discovery of the individual who is particularly susceptible to noise is desirable, but satisfactory predictive tests are not yet available, and serial audiometry is necessary—due account being taken of normal ageing. "A noise analysis alone will only indicate the *potential* hazard. The *actual* hazard must be directly measured . . . by . . . audiometry".

R. Hinchcliffe and T. S. Littler have drawn on their experience to produce a most practical paper (*Methodology of air-conduction audiometry for hearing survey*, pp. 114–33) which is required reading for anyone who has embarked or is about to embark on a programme of audiometry. The characteristics of audiometers, and sources of fluctuation in output are described, and the

need for regular monitoring and calibration is made apparent. The requirements in regard to ambient noise for accurate audiometry are discussed. (In an Appendix, G. F. PENNINGTON gives details of materials and construction of a mobile audio test chamber.) The procedure for determination of threshold is described.

The Scottish Audiometer Calibration Service is described by E. C. KNOX and J. M. A. LENIHAN (pp. 104–13). The Service has been established jointly by the Department of Health for Scotland and the Western Regional Hospital Board, the latter body defraying the running costs. Calibration and any necessary repairs are normally completed within 24 hours. The main tests made are (1) measurement, with artificial ear, of output levels at indicated hearing loss of + 60 dB for each earphone and each frequency, (2) measurement of each output frequency, and (3) measurement of all attenuator steps between 0 and + 60 dB at 125, 250 and 8,000 c/s. The results of the tests on the first 50 audiometers give a convincing demonstration of the need for the Service.

The symposium includes 2 reports of field studies. In the first, *A study on occupational deafness in the Netherlands*, by H. A. VAN LEEUWEN (pp. 90–97) an analysis is presented of the results of 300 audiograms from workers in various departments of 7 factories. The environmental sound levels ranged from about 85 to 115 dB. Continuous audiometry was employed, and the results were expressed in the form of a degree of damage index derived from the depth and width of the typical noise induced "dip". The degree of hearing damage appeared to be correlated with noise spectrum level, and definite trauma was found where the total noise level exceeded 90 dB. Young workers were found to show a greater temporary loss as the result of a day's exposure than did those with longer exposure history, but the evening audiograms for both groups were similar. R. R. A. COLES and J. J. KNIGHT, in their contribution, *Auditory damage in young men after short exposure to industrial noise* (pp. 98–103) examine the audiometric data obtained from 111 young naval recruits, 30 of whom had been engaged only in quiet occupations, or had recently left school. 10% of the group had a history of work in extremely noisy surroundings, and they showed a hearing loss at 4,000 c/s which was 6·4 dB greater than that occurring in a control group. Altogether, at least 13% of those examined had a detectable hearing loss considered to be due to industrial noise trauma. Attention is drawn to the possible hazard to the noise-susceptible individuals who fire small-arms as a sport.

D. M. A. MERCER provides an interesting description of a technique which has been developed for use in the field of communications science, but which appears to be potentially useful in many problems of noise measurement and analysis (*The application of correlation techniques in noise analysis*, pp. 81–89). An electronic correlator may be used to obtain information from 2 apparently unrelated functions by introducing a variable delay between them, then obtaining the product of the 2 functions, integrating and then averaging. Examples given of possible uses of this technique include location of noise sources and determination of the acoustic attenuation of panels.

Machinery and processes which produce noise are almost certainly also sources of vibration, which may in itself have an adverse effect upon human health and comfort. The article by G. G. PARFITT entitled *The analysis and control of vibration* (pp. 68–80) is thus a timely contribution to the symposium. A description is given of the principles of vibration measurements, and this is followed by a discussion of levels of vibration which should not be exceeded if human discomfort, damage to building structures, and metal fatigue are to be avoided. The effects of vibration may be minimized by measures similar to those used in the case of noise, *i.e.* by wise planning; reduction of vibration at source; insertion of absorbents in the surroundings of, or the transmission path between, source and observer; and the insertion of a reflecting barrier in the transmission path.

D. E. Hickish

CROUCH, H. W. & ANDREWS, D. **Reduction of Air Flow Noises.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 514–19, 8 figs.

Compressed air jets used for cleaning purposes or for the ejection of small parts can produce high noise levels, often with considerable energy in the upper frequencies. When the air stream impinges on a target the noise level may be greatly increased. Sound levels are given in relation to pressure drop for 4 sizes of circular nozzles ranging from $\frac{1}{8}''$ diameter to $\frac{5}{16}''$ diameter, and for slot nozzles $\frac{1}{8}'' \times \frac{7}{8}''$ and $\frac{3}{32}'' \times 1\frac{1}{2}''$. Corresponding data are given, for the circular nozzles, of the sound levels produced when the air jet is directed against steel block and mesh screen targets.

The noise produced during the air ejection of parts can be reduced by lowering the air pressure, although this may involve the necessity for modification of the machine to ensure that removal of the parts from the die remains efficient. Where the jet is not used for ejection, but is merely the exhaust from an air operated mechanism, a silencer should be fitted,—noise reductions from 118 db to 82 db have been experienced.

Briefer references are made to the reduction of noise in an air drying machine, and in ventilation systems.

D. E. Hickish

YOUNG, R. L. **Some Noise Control Methods used in Industrial Operations.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 520–27, 7 figs.

One of the most successful ways of controlling the exposure to noise from existing machinery is to control the transmission path of the air-borne sound. An example is given of an enclosure built round a tumbler, which reduced the overall noise level from 111 db to 88 db, with reductions of 22 to 24 db in each of the important 4 octave bands between 600 and 10,000 c/s. Where machinery is large, the provision of a sound insulated control booth for the protection of the operators may be a preferable approach. Details are given of an air-conditioned observation booth with large windows, for the use of paper machine operators. The overall noise exposure outside the booth of 108 db was reduced to 88 db inside the booth, and the octave band levels were reduced by 20 to 25 db. In

other instances enclosure of a noisy machine and its operators (who must of course be provided with ear protection) will reduce the exposure of other personnel in the workshop.

Where complete enclosure is not practicable owing to the need for openings, *e.g.* for conveyors, the size of the opening will be the factor limiting attenuation, and should be kept as small as possible. Curtains of rubberized canvas help to reduce the noise through the necessary openings. A partial enclosure of this type when applied to a small foundry shake-out gave a maximum noise reduction of 7 db in overall level with reductions from 96 db to 86 db in the critical frequency band levels in the 600 to 1,200 and 1,200 to 2,400 c/s bands, at a point 6 feet to the side of the enclosure.

Sound barriers are less effective than enclosures, and as the dimensions of the barrier must be several times the wavelength of the sound, their usefulness is often limited to the higher frequencies. Noise levels at a point 10 feet behind a radial saw were reduced by about 10 db in octave bands between 600 and 10,000 c/s by the erection of a barrier 8½ feet high and 24 feet wide.

Vacuum pumps, blowers and air operated equipment often produce levels of noise which are very high, but which can be reduced by snubbers and mufflers, and several examples of this type are given in the paper. Typical reductions are 120 to 102 db, 116 to 101 db, and 114 to 88 db. The replacement or partial replacement of metal gear drives by non-metallic gears or fluid drive transmission systems has given useful noise reductions (*e.g.* 95 db to 83 db).

A change in process, *e.g.* from pneumatic hammering to the use of pinch roller machines for metal bending, may eliminate a noise problem which would otherwise be very difficult of solution. *D. E. Hickish*

STROHMENGER, P. & GRÜN, L. Weitere Untersuchungen über die Gesundheitsgefährdung von Hitzearbeitern. [**Further Investigations on the Health of Workers exposed to Heat Radiation**] *Arch. f. Hyg. u. Bakt.* 1959, Apr., v. 143, No. 3, 161–71. [12 refs.]

In this paper which follows a previous one on the same subject the authors analyse the sickness experience of workers exposed to high temperatures in respect of the nature, frequency and duration of illness. The data from 3 groups of workers were considered. The groups were: (1) 231 men directly exposed to high temperatures in a steel works who worked on an 8-hour changing shift system, (2) 185 men, also on changing shift work, who worked in association with the actual steel production but were not directly exposed to the heat radiation as were group one, and (3) 247 workers who were not exposed to heat and worked only for the early 8-hour shift from 6 a.m. to 2 p.m.

The results of the investigation are described with several statistical tables and are discussed with reference also to other published work. The main finding was that disorders of the stomach and intestinal tract were equally frequent in groups 1 and 2 and that this prevalence was about double that experienced in group 3. No statistically significant differences were found between the 3 groups in respect of the prevalence of diseases of the liver, gall-bladder, kidney, skin, heart and circulation. It was also found that in workers exposed to strong heat radiation there was frequent retirement from work before reaching the age of 65 years and also frequent change of employment which are regarded as evidence of premature loss of working capacity. *M. E. Delafield*

BORNEFF, J. Untersuchungen zur Wärmestrahlenbelastung im Eisenhüttenbetrieb. [**Investigations on Heat Radiation in an Ironworks**] *Arch. f. Hyg. u. Bakt.* 1959, Jan., v. 143, No. 1, 1–20, 6 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The importance of heat radiation in medicine also in regard to the carcinogenesis has been discussed. The climatic conditions and the heat radiation have been determined at different sites of an iron works. The maximum intensity of radiation amounting to 0.65 watt/cm² has been found at the blooms-shears. The average radiation to which the workers were exposed during a working day amounted to 1500–5000 watt/sec/cm². The energy of the infrared radiation was distributed differently into the short and long wave part of the infrared depending upon the working place examined. The greatest part of the energy of the short wave infrared radiation up to 1400 mμ (this is the radiation which invades the tissue) was emitted by the molten iron during tapping from the blast furnace."

BORNEFF, J. Über die Wärmestrahlung besonders in Glashütten. (Messergebnisse und physikalisch-medizinische Grundlagen.) [**Heat Radiation particularly in Glass Works**] *Arch. f. Hyg. u. Bakt.* 1959, June, v. 143, No. 4, 241–61, 6 figs. [Numerous refs.]

In a previous paper the author reported on his investigations on heat radiation and the atmospheric conditions of temperature, humidity and air velocity in an iron and steel works [see above].

The present paper reports the results of the same methods of examination in 2 glass works. There is an account of the different processes of glass manufacture in these works which is followed by a description and discussion of the literature on the diseases of glass workers. These diseases are considered in separate sections on: (1) the general diseases among which are those of the respiratory system, the skin and the digestive system and also rheumatism and cardiac disease, (2) the association of heat radiation and cancer. This subject is discussed at length although the author found no evidence of such an association in glass blowers and (3) the incidence of cataract in workers in glass and other industries.

Physical measurements were made at many different points in the 2 glass works and for comparison in a domestic kitchen. These are set out at length with tables and figures. It was determined that glass blowers working near the melting furnace receive a daily dose of radiation of 2,000–3,000 watt/sec./cm² of which

about 10% is infra-red radiation of wave lengths smaller than 1,400 mμ. This amount of radiation is acually less than that to which blast-furnace workers in iron-works had been shown to be exposed yet the incidence of cataract in these iron-workers is less than in glass blowers. To explain this the opinion is expressed by the author that cataract is caused, not by the direct effect of infra-red radiation on the lens, but probably by the continual heating of the tissues of the eye by hot air, for it was shown that air temperature was much higher for the glass workers than for the blast-furnace workers.

The general results are discussed. *M. E. Delafield*

RAFFLE, P. A. B. **Medical Examinations for Public Safety.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 98–103. [12 refs.]

In this paper the medical standards for bus driving in London are briefly re-stated with some stress on the various conditions which may cause sudden loss of consciousness while driving [this *Bulletin*, 1955, v. 30, 39; 1959, v. 34, 132]. Information is presented on the clinical conditions most frequently recorded as the reason for exclusion from driving, as determined by the doctors working in London Transport.

In a table there are given the results of pre-employment medical examination of 18,003 applicants in the period 1950–57. The applicants were self-selected by inclination to be a driver and in the knowledge that a medical examination to a public safety standard was involved and selected by interview and by previous driving experience. Yet 3,367 (18·6%) were rejected. Of these rejections 2,321 were due to sub-standard vision or colour vision, 245 to cardiovascular disorders, 149 to pathological conditions of the ears, mainly chronic otitis media, and 100 to defective hearing. Particulars are given of the other medical or surgical reasons for rejection. Other tables set out the findings at routine medical examinations which were carried out for various reasons during employment.

The conditions which render a man unfit for a job involving public safety are shortly described and discussed. *M. E. Delafield*

JONES, G. Mary. **Incapacity for Work among the Insured Population of Great Britain.** *Brit. J. Preventive and Social Med.* 1959, Apr., v. 13, No. 2, 74–87, 4 figs.

"The Ministry of Pensions and National Insurance usually receives between eight and nine million new claims for sickness and injury benefits in a year and records certified incapacity for work totalling nearly 300 million days. Detailed analyses are made from the records of spells of incapacity for work in respect of 5 per cent. of the insured population." The latest of these analyses, available to research workers on application to the Ministry, are entitled "Digest of Statistics Analysing Certificates of Incapacity, 1954–55 and 1955–56".

This paper contains tables and charts which illustrate the position shown by the figures in one or both of those periods. The statistical data are set out in much detail. They concern the number of the home population by age and sex and estimated numbers insured for benefit; extent of claims for sickness benefit; numbers of claimants incapacitated by duration of spell of incapacity; extent of incapacity for work in different age-groups; regional analyses of men claiming sickness benefit; days of incapacity for work analysed by causes (WHO detailed list); number of persons experiencing industrial accidents and work days lost through different types of industrial accidents; and prescribed industrial diseases in stated industries. *M. E. Delafield*

MÜNK, H. [Edited by.] Rehabilitation. Vorträge der Tagung der Werksärztlichen Arbeitsgemeinschaft in Nürnberg vom 2. bis 4. Oktober 1958. [**Rehabilitation Lectures at the Congress of the Industrial Medical Association in Nürnberg, 2nd–4th October 1958**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Suppl. No. 5, pp. x + 152, numerous figs.

This fifth Supplement to the *Zent. f. Arbeitsmed. u. Arbeitsschutz* contains 14 papers on various aspects of Rehabilitation, which was the main subject chosen for the conference of the Industrial Medical Officers Association held in Nuremberg in October 1958.

In the first paper the author (E. HOESCHEL—"*Rehabilitation in angelsächsischen Ländern*" [Rehabilitation in Anglo-Saxon Countries], pp. 1–11) reviews from his own observations the basic principles of rehabilitation as they are understood in the United States of America and in England and gives some description of the methods whereby rehabilitation is carried out and of the minor differences between these in the 2 countries. Rehabilitation in Germany was the subject of the succeeding paper (J. F. SCHOLZ—"*Die Rehabilitation in Deutschland*" [Rehabilitation in Germany], pp. 11–24) in which tribute was paid to the excellence of the methods employed in Anglo-Saxon countries but it was also maintained that Germany, by its legal enactments in respect of disabled persons, the first of which dates from 1923, was the pioneer in this field. The magnitude of the problem of rehabilitation in Germany is indicated by these approximate figures of disabled persons: about 1,100,000 persons with tuberculosis of whom over 100,000 have active disease; 3,710,000 disabled people in receipt of war pensions; accidents of all kinds cause annually 3;000 total and 350,000 to 400,000 partial disablements; there are very large numbers of congenital or acquired disabilities. The methods of coping with the problem of rehabilitation in Germany are described.

In an excellent paper (G. WAHL—"*Erhaltung von Arbeitskraft und Arbeitsplatz*" *aus der Sicht der Rentenversicherung* [Maintenance of Capacity for Work and Employment from the Insurance Aspect], pp. 24–45) the subject of the maintenance of capacity for work and continuation of employment in industry is considered from a number of points of view including that of insurance and its reform. Statistics are given of the mortality experience and of the frequency of the chief causes of premature invalidism. To lessen this burden there should be a much greater development of various measures for early treatment, particularly of workers with disorders of the heart and circulation, to prolong their period of industrial efficiency. Extension of the

work of the industrial medical service in various directions is also needed. Among other subjects which are dealt with are the employment of severely disabled persons in industry and the rehabilitation or re-education of those who have become partially disabled from a variety of causes.

The problem of the employment of severely disabled persons was partly solved by an Act (*Schwerbeschädigtengesetz*) which came into force in 1953 and imposed on employers the duty of engaging a certain percentage of such persons on their staff. The experiences of the working of this Act are described. The numbers of severely disabled persons in Western Germany and West Berlin has been reduced from over 48,000 in 1953 to about 20,000 in 1958. (M. HOFRICHTER—"*Aktuelle Fragen zur Durchführung des Schwerbeschädigtengesetzes*" [Current Position of the Working of the Law Relating to the Severely Disabled], pp. 45–50.)

In 2 short papers some points in the rehabilitation of young people with physical handicaps for employment are considered (F. BECKER—"*Eingliederung von jugendlichen Körperbehinderten ins Erwerbsleben*" [Arrangements for Physically Handicapped Young Persons in Employment], pp. 50–52), with special reference to various occupational disorders of the spinal column (F. BECKER—"*Rehabilitation von Wirbelsäulengeschädigten*" [Rehabilitation in Spinal Injuries], pp. 52–53).

The special problems which exist in the rehabilitation of the female are considered in regard to her anatomy, physiology and disposition in a paper in which there is some description of the important clinical conditions and their treatment (H. W. VASTERLING—"*Rehabilitation bei Frauenkrankheiten*" [Rehabilitation in Diseases of Women], pp. 53–59).

Tuberculosis still presents great problems in the rehabilitation of sufferers. In a paper on this subject (D. SCHWENKENBECHER—"*Letztjährige Erfahrungen über die Arbeitstherapie und Rehabilitation bei Lungenkranken*" [Recent Experience in Occupational Therapy and Rehabilitation in Pulmonary Diseases], pp. 59–67) some figures of incidence are that at the present time about 23 new infections per 10,000 of population are discovered, which is, however, a great improvement on the 56 per 10,000 recorded in 1949. The recent experience of methods of rehabilitation of tuberculous persons in Germany is described.

A paper on modern orthopaedic aids and technical devices (W. PIEPER—"*Orthopädische Versorgung und Wiedereingliederung von Armversehrten*" [Orthopaedic Care and Technical Aids for Arm Injuries], pp. 67–75) for use by workers who have disabilities, such as amputations, of the upper limb contains a good general description with illustrative photographs. The author remarks that it can be stated without exaggeration that persons with disabilities of the arm can be employed in practically every occupation.

The maintenance of health in the mining industry of the Ruhr is described and discussed in a paper with a good summary by the author of his 5 years of experience (A. VON GEISO—"*Massnahmen zur Gesunderhaltung im Ruhrbergbau*" [Maintenance of Health in the Ruhr Mines], pp. 75–83).

The importance of the psychiatric viewpoint in rehabilitation is discussed in a long paper (F. W. BRONISCH —"*Rehabilitation—psychiatrisch gesehen*" [Psychiatric Aspects of Rehabilitation], pp. 83–95) in which the author speaks of the need for psychiatric expert knowledge in dealing not only with psychiatric cases but also with persons who through physical disablement, disease, old age and social causes are psychologically disturbed.

The special problems inherent in the employment of persons with cerebral damage were also considered and discussed at some length by H. H. HEINSOHN in his paper—"*Neurologisch—psychiatrische Probleme des Arbeitseinsatzes Hirnverletzter*" [Neurological and Psychiatric Problems of Brain Injuries of Occupational Origin], pp. 96–104.

The organization of industry in such a way that the health and strength of the workers are maintained while keeping output at a high or increasing level is described and discussed in 2 papers of some considerable length. In the first of these papers (B. SCHULTE—"*Prophylaktische Arbeitsgestaltung in der Industrie*" [Preventive Measures for Working Conditions in Industry], pp. 104–120) the subject is considered in general terms and reference is also made to the importance of constructing machines in such fashion as to lessen as far as possible the human effort needed for their working, particularly because the speed of production is ever increasing. The second paper (A. WIEDEMANN—"*Prophylaktische Arbeitsgestaltung aus psychologischer Sicht*" [Preventive Measures for Working Conditions from the Psychological Aspect], pp. 120–132) contains a long account of the psychological aspects of industrial organization such as the response to stimuli for maintaining production, concentration and perception and the psychic components of the different movements carried out while at work.

The last paper (J. BERNING—"*Die Anpassung von Arbeitsplätzen an die Leistungsfähigkeit Körperbehinderter*" [The Adaptation of Work Places for the Productivity of the Physically Handicapped], pp. 132–147) contains a good account with some clear diagrams of methods whereby places of work can be adapted in such a way that physically handicapped persons can carry out productive work. The rehabilitation of these persons, their difficulties and the ways in which management and the industrial medical officer can help them are also described. *M. E. Delafield*

ARNULF, A., BRICARD, J., BURTIN, R. & VERET, C. Étude de la granulomètrie des brouillards par photographie directe des gouttes liquides en suspension dans l'air. [**Measurement of Droplets in Clouds by Direct Photography of Liquid Drops Suspended in Air**] *Ann. Occup. Hyg.* London. 1959, Apr., v. 1, No. 2, 162–79, 16 figs. (2 on pl.).

The English summary appended to the paper is as follows:—

"In an introductory section the methods of sizing clouds of droplets are outlined, the difficulties of direct photography of drops in air are pointed out and an apparatus specially designed for the study of drops composed of volatile liquids is described. In this apparatus the drops are photographed as they are swept by a jet of air through the field of view of a microscope, the illumination being at right angles to both air movement and the axis of the microscope.

"In the second part the appearance under the microscope of a water droplet illuminated laterally is interpreted: three parts of the image appear bright, one corresponding to light externally reflected by the drop, one to light directly transmitted and one to light transmitted after two internal reflexions. The brightness of these three images is calculated on the basis of Wiener's theoretical results.

"Finally, the appearance of the images obtained with the proposed apparatus is explained, and its performance compared with those of normal methods."

MANSUR, R. H., PERO, R. F. & KRAUSE, L. A. **Vapor Phase Chromatography in Quantitative Determination of Air Samples collected in the Field.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 175–82, 6 figs. [13 refs.]

"Progress in development of a method of using vapor phase chromatography for the quantitative determination of solvent vapors in air has been described. It is concluded that, in the present stage of development, the method is usable from the standpoints of accuracy, specificity, time requirement, and cost. It is emphasized, however, that certain features of the method should have further study. It is also believed that, with further study by other interested groups, the general principles of the method can be modified to fit numerous other needs of the industrial hygiene profession."

PNEUMOCONIOSIS ABSTRACTS. Vol. III Reproduced from the *Bulletin of Hygiene* for the years 1951 to 1955 inclusive. pp. viii + 376. 1959. London: Pitman Medical Publishing Co. Ltd., 39, Parker Street, W.C.2. [for Bureau of Hygiene & Tropical Diseases]. [65s.]

Between 1934 and 1937, DAVIS, SALMONSEN and EARLYWINE published their 3 volumes of *The Pneumoconioses (Silicosis) Literature and Laws*. These books attempted, very successfully, to cover the world's literature on dust disease, and they were of immense help to all workers in the pneumoconiosis field. Enquiries after the war, in Chicago, where the books were published, elicited the information that it was not intended to pursue the project, and that there would be no further volumes of *The Pneumoconioses*. This was a great disappointment to all physicians, pathologists and engineers concerned. Representations were then made on behalf of the Pulmonary Diseases Committee of the Medical Research Council in Britain to the Bureau of Hygiene and Tropical Diseases to explore the possibility of reprinting in book form the excellent abstracts of pneumoconiosis papers which had been appearing in their *Bulletin of Hygiene* since 1926. It is a tribute to the vision of the Director and the Honorary Managing Committee that they saw at once what a great service to an important branch of medicine would result from the publication at regular periods of abstracts of the world's medical, scientific and engineering literature in this field. Published by Pitmans, in well set-out books, these collected abstracts give immediate and easy access to everything that has been written on the subject. As the coverage of the *Bulletin of Hygiene* is very wide, these volumes of their collected abstracts can be confidently regarded as a *complete* account of everything worthwhile that has been published. The abstracts are grouped by subject and cross references are given to related topics.

Previous volumes (I and II) [this *Bulletin*, 1954, v. 29, 284, 953] contained all pneumoconiosis abstracts printed in 1926–40 and 1940–50.

Volume III of *Pneumoconiosis Abstracts* covers the years 1951–55. It is uniform in size and binding with the previous volumes. The classification of the contents has been modified: the single section formerly devoted to silicosis has been broken up into 4 sub-headings; asbestos and asbestosis have been included with other silicates; coal and graphite pneumoconioses have been grouped together; and a new section is devoted to pneumoconiosis of foundry workers and welders. The general section and the sections devoted to other inorganic and to organic dusts remain. The 2 final sections in the table of contents are *Dust Sampling and Analysis* and *Dust Control*. These alterations strike one as being both reasonable and useful, and should make general browsing through the volume more profitable.

As is pointed out in the foreword, there is some lack of uniformity in the printing type because this volume was produced by a photographic process from the original abstracts, but this does not detract from the appearance of the volume.

The abstracts are those found in the *Bulletin of Hygiene* and as usual are signed. The abstracters are well practised in their art and much material is presented in a concise and lucid fashion.

There are 2 indices, one of authors and sources, and one of subjects. They both seem accurate and reliable, and the latter of the two enables the subject matter to be quickly and easily located.

These 3 volumes are undoubtedly of very great value to all those who are interested in the pneumoconioses, rendering a large mass of literature readily available quickly, easily and efficiently. No laboratory and no bookshelf of any worker in this field is complete without them. *E. J. King*

CENTRAL MINING — RAND MINES GROUP. HEALTH DEPT. **Report for the Year 1958** [COETZEE, A. M., Chief Medical Officer]. 24 pp., 2 folding charts. 1959. Johannesburg.

The Central Mining—Rand Mines Group operates goldmines and 3 coalmines on the Witwatersrand and in the Orange Free State. During 1958, 75,797 Africans were employed at the goldmines but in the same period there were 84,020 new recruits representing a labour turnover of 111%. The mining companies maintain a comprehensive full-time medical service based on mine hospitals comprising 2,021 beds. After 40 years Dr. A. J. ORENSTEIN, one of the leading tropical hygienists of modern times, retired from the post of chief medical officer of the group. On 15 April, 1958, the native hospital at Blyvooruitzicht, which now bears his name, honoured him by unveiling a portrait plaque.

In the annual report for 1958 Dr. A. M. Coetzee gives comprehensive morbidity and mortality statistics of Africans. Mortality trends of accidents, pneumonia and

tuberculosis are presented graphically for the period 1910 to 1958. It is a record of gradual but steady improvement.

Among occupational diseases there were 14 cases, 4 fatal, of heat stroke arising out of employment in the mines. 74 cases of pneumoconiosis were diagnosed among natives employed in the goldmines; in no less than 38 (51%) of these cases the pneumoconiosis was accompanied by tuberculosis. Only 1 case of pneumoconiosis occurred among the 3,150 African coalminers.

All mines are now equipped to carry out the radiographic requirements of the Pneumoconiosis Act. The members of the medical and technical staffs work in close collaboration with the Pneumoconiosis Research Unit of the Council for Scientific and Industrial Research. *A. Meiklejohn*

CARSTENS, M., BRINKMANN, O., LANGE, H. J., MEISTERERNST, A. & SCHLICHT, H. Die Staubschädigungen der Bergleute. [**Dust Disease of Miners**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 1, 67–107, 11 figs. [Numerous refs.]

This long paper presents the clinical and physiological findings in a group of 623 compensated miners. 404 had silicosis (146 stages I and II and 258 stage III) and 219 were free from silicosis but had bronchitis and emphysema, heart and circulatory disorders and other miscellaneous conditions. These groups are compared and the results given in a number of tables. The authors conclude that miners' lung function declines earlier and more rapidly than that of other workers and that this decline is not closely related to a diagnosis of silicosis or bronchitis and emphysema but depends on the length of time worked in the industry; simple silicosis causes no reduction in lung function, while massive fibrosis reduces function in proportion to the size of the mass; and that bronchitis and emphysema are independent of the presence or stage of silicosis.

These conclusions are discussed in the light of a system of compensation based on radiographic evidence of silicosis and the authors express the view that miners' dust disease is the sum of all reactions of the organism to dust, including physical and chemical irritation of the bronchi and alveoli leading to bronchospasm, asthmatic bronchitis, emphysema and bronchiectasis.

I. T. T. Higgins

VIGLIANI, E. C. & PERNIS, B. **Immunological Factors in the Pathogenesis of the Hyaline Tissue of Silicosis.** *Indust. Med. & Surgery.* Miami. 1958, Dec., v. 27, No. 12, 643–5. [24 refs.]

The evidence is presented for a possible immunological origin of hyaline tissue in silicosis corresponding to an antigen-antibody reaction. The first evidence was provided by the finding of similar chemical compositions of hyaline and amyloid. Secondly, with the technique of GRABAR and WILLIAMS (*Biochim. et Biophys. Acta,* 1955, v. 17, 67), a single type of rabbit serum antibody against normal human serum was shown to be removed by absorption with silicotic tissue. This antibody reacted with the beta and gamma globulins. Control normal lung tissue failed to absorb the antibody. Thirdly, homogenized silicotic tissue, injected intraperitoneally into rabbits, produced an antiserum which reacted with normal human serum electrophoretically separated in an agar plate giving a single line of precipitation through the beta and gamma globulins. Thus the acellular hyaline tissue can be assumed to contain a globulin fraction similar to that having antigenic properties and having the electrophoretic mobility of beta and gamma globulin. Fourthly, the increased globulin in the blood, the increase of plasma cells and histiocytes in the reticulo endothelium system, the progressive nature of silicosis and the different reactivity of man to silica are points of similarity of silicosis with the "collagen diseases". Quartz may act similarly to Freund's adjuvant.

On the basis of this work the authors suggest 4 possible hypotheses: (a) silica itself is an antigen, (b) silica induces formation of auto-antigens, (c) silica acts as an adjuvant of hetero-antigens, and (d) silica sets auto-antigens free by killing a larger number of cells. The immunological hypothesis provides a new field of research.

[This is a brief outline of work which has already been more fully reported, see VIGLIANI *et al.*, this *Bulletin*, 1950, v. 25, 1147; GLYNN and HOLBOROW, *ibid.*, 1953, v. 28, 65; JÄGER, *ibid.*, 1955, v. 30, 385; SEIFERT, *ibid.*, 386; PERNIS, *ibid.*, 1956, v. 31, 541, 828. It promises to be a most encouraging step forward in the study of pneumoconiosis.] *D. Rivers*

PERNIS, B., GAMBINI, G. & LEVIS, F. **A Heat-Labile Zymosan Agglutinating Factor observed in Rabbits after Intravenous Injections of Quartz.** *Proc. Soc. Exper. Biol. & Med.* 1959, Jan., v. 100, No. 1, 49–53. [14 refs.]

Sera of rabbits which had received several intravenous injections of quartz were found to contain an agglutinating factor (quartz factor, QF) for zymosan. After testing 3 different zymosans, zymosan G-6 was found to give the best results. Out of 10 rabbits which had received quartz injections, 8 sera gave agglutination of zymosan to titres of 1 in 128 and 1 in 256. The sera of uninjected controls did not agglutinate zymosan. Sera of untreated farm-bred rabbits, however, were found to agglutinate zymosan at titres of 1 in 64 and 1 in 128. Among 4 laboratory stocks of uninjected hybrid rabbits zymosan agglutination occurred with 41% of sera of one stock and with 50% of a second stock; no agglutination was produced by sera of the two other stocks.

The relationship of QF to properdin and bovine conglutinin was next investigated and QF was found to differ from both these factors. Thus QF was inactivated by heating at 56°C. for 30 minutes, and by typhoid endotoxin and hog gastric mucin. QF agglutinated zymosan at ionic strengths of 0·69 and was not eluted. As for conglutinin and properdin, the presence of divalent cations was found to be necessary for agglutination of zymosan by QF. QF serum, either fresh or inactive, did not conglutinate sheep red cells treated by method I of Coombs and Coombs. QF was also found to differ from immunoconglutinin; the latter probably accounted for agglutination of zymosan by the sera of some of the

uninjected "normal" stock rabbits. In some QF sera the titre of agglutination was reduced by heating to 56°C. so that QF may co-exist with immunoconglutinin. QF is not related to Cx-reactive protein as the latter does not agglutinate zymosan.

The authors conclude that QF does not behave as a classical antibody but that it acts in some ways like properdin and in other ways like a conglutinin. The cause of QF is not known and it may not be specific for quartz. Quartz may act directly or indirectly by damaging cells.

[This is an interesting aspect of the new immunological hypothesis of silicosis developed by the Italian school.] *D. Rivers*

KERN, R. Vergleichende tierexperimentelle Untersuchungen mit quarzhaltiger Asche aus akuten und chronischen Lungensilikosen. [**Animal Experiments with Quartz-Containing Ash Obtained from the Lungs of Acute and Chronic Silicotic Subjects**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 1, 108–16, 3 figs. [Numerous refs.]

The object of the experiments was to use the actual quartz-containing dust extracted from lungs affected by acute and by chronic silicosis to test whether acute silicosis is due to the inhalation of a large amount of quartz for a short time or to the inhalation of freshly fractured quartz. One group of rats was given the ashed dust from an acute silicotic lung and another group the dust from a chronic silicotic lung. Some rats received the dust by intraperitoneal injection and some by intratracheal injection. A control group of rats received ashed dust freed from quartz. Equal doses of each dust were injected into the separate groups and animals from each group were sacrificed at the same time intervals after injection.

The amount of fibrosis produced by each dust was proportional to its quartz content and to the period after injection. No differences were observed between the ashed dusts obtained from the acute and chronic silicotic lungs. The quartz-free dust produced no fibrosis. The results provide further evidence against the hypothesis of an enhanced fibrogenic property of freshly fractured quartz as compared with aged quartz. Quartz particles under 3μ in size were found to be the more fibrogenic, which is in accord with results of other workers. *D. Rivers*

IGAKU KENKYU. Fukuoka. 1958, Dec., v. 28, No. 13, 1–240, illustrated. [Numerous refs.] [**Papers on Experimental Silicosis**] [In Japanese.] English summaries.

[Pneumoconiosis affects workmen in mines and factories in countries throughout the world. The disease, wherever it occurs, attracts scientific study. Owing to language difficulties the results of these enquiries are not easily made universally available. As a means of surmounting this difficulty of exchanging knowledge, it has become increasingly common in recent years to include with the original article an abstract or summary in one or more foreign languages. Unfortunately, the service is all too often diminished by the inadequacy of the abstracts and the translation. This criticism is not intended to discourage what is a real advance in medical papers but to emphasize the need for editors to improve the standard of the actual abstracts which are often too brief to be informative, and to assure competent technical translation, which is an even more difficult matter.]

An extensive programme of pneumoconiosis research is in progress at the Medical Research Institute for Industry and at the associated hospital of the Tagawa colliery, Mitsui, Japan. The following 13 papers, which occupy 240 octavo pages, record the results of laboratory studies of the pathogenesis of pneumoconiosis due to a variety of dusts.

I. MATSUOKA. On the Relationship between the production of Antibody and the Patho-histological Appearance of Lung, Liver and Spleen in Rabbit Injected Rock Crystal Intravenously (pp. 1–40).

Suspensions of rock crystal dust were injected intravenously into rabbits. The injections varied in quantity and in size of particles, and in the period over which they were maintained. The animals were divisible into 2 main groups according to whether they were injected during the summer months or other months of the year. 2 forms of rock crystal were used; coated and non-coated with rabbit serum protein. Among the non-summer group of rabbits antibody production reached its highest point after 12 to 16 weeks but in the group injected in the summer the maximum agglutination titre developed after 4 to 8 weeks. The author concludes that hyaline degeneration in silicotic nodules is due to an antigen-antibody reaction. No significant difference in antibody production was observed between the serum-coated and non-coated particles.

Y. SHOYAMA. A Study on the Protein Adsorption of Silica and the Alteration of Protein Adsorbed on it (pp. 42–55).

Suspensions of protein-coated and non-coated rock crystal dust were injected into the ear vein in rabbits. Both suspensions produced antibodies which were measured. When silica adsorbs serum protein the β globulin fraction is first adsorbed and then successively albumin, α_1 globulin, α_2 globulin and finally γ globulin.

H. KOOZAKI. Studies on Denaturation of Protein Adsorbed on Silica (pp. 56–64).

Rock crystal, quartz and other forms of silica rock were used as antigens. The experiments confirmed that the denatured protein consists of 3 fractions, the first specific to the particular dust, the second common to quartz and silica rock and the third common to rock crystal and silica rock.

M. NAGAE. Studies on the Production of Antibody by Mixed Siliceous Stones Administered Parenterally (pp. 65–79).

4 varieties of silica dust were injected parenterally into rabbits. A common antibody and specific antibodies developed. The author concludes that the solubility theory is not adequate to explain the production of these different antibodies.

T. Nomiyama. The Formation of Silicotic Nodules in the Rabbit Sensitized with Rock Crystal (pp. 80–90).

The observations of other workers that histological changes vary between sensitized and non-sensitized rabbits were confirmed.

Y. Watanabe. Immuno-histological Studies on the Rabbit Sensitized with Rock Crystal (pp. 95–110).

This contribution is substantially similar to the above.

Y. Tahara. Studies on the Agglutination Reaction of Serum for 6 Kinds of Silica Antigen, in Healthy Humans and Labourers Working in the Dusty Atmosphere (pp. 113–32).

This is a field study in extension of the fundamental laboratory investigations of Nomiyama and Watanabe. Human serum was found to contain antibodies which have power to agglutinate 6 different silica antigens. The agglutination titre is higher in women than in men. The conclusion is that among workers in dusty occupations, who have a high agglutination titre for silica antigen, silicotic nodules will be formed immediately upon inhaling the appropriate silica dust. Accordingly the observed differences in development of silicosis, including acute silicosis, among workmen similarly exposed to the inhalation of silica dust, may be explained immunologically.

S. Miyazaki. Inhibitory action of Vitamin B_1 against the Formation of Silicosis (pp. 134–48).

Vitamin B1 was administered orally and subcutaneously to mice previously injected intraperitoneally with rock crystal. The formation of silicotic nodules was not prevented but was diminished.

T. Nakamura. A Study on Antibody produced by the Intravenous or Subcutaneous Injection of the Various Kinds of Coal Mine Sandstone (pp. 149–65).

17 different samples of coalmine rocks were used as antigens. The experiments and results accord with those of preceding contributors.

G. Fujisawa. Serological Studies on the Rabbit Serum injected Zettlitz Kaolin (pp. 166–84).

To test the pathogenic action of kaolin, suspensions of this material, some pure, others treated to 700°C. for an hour, were injected subcutaneously and intraperitoneally into rabbits. Apart from a slight foreign body reaction neither form of kaolin produced fibrosis and there was no production of antibody in the rabbit.

S. Kondo. Serological Study on Rabbit Serum Injected Ion Exchange Resin Subcutaneously (pp. 185–203).

No fibrosis was produced in rabbits by subcutaneous injection of various ion exchange resins. Protein was adsorbed but there was no evidence of significant denaturation.

M. Ooba. Serological Studies on the Experimental Asbestosis (pp 204–23).

This study is similar to those already noted except that the dusts used were composed of several varieties of asbestos.

M. Koga. On the Formation of Antibody and Alteration of Tissue by the Parenteral Administration of Mixed Suspension of Graphite and Rock Crystal and of Sandstone and of Rock Crystal and Anthracite (pp. 225–40).

Immunological and histological observations were made on rabbits and mice injected parenterally with suspensions of graphite, rock crystal, anthracite and sandstone in various combinations. The author concludes that graphite does not injure the protein, does not enhance the protein reaction of rock crystal and does not cause any specific fibrosis.

[This brief survey does not claim to provide research workers with precise details of the experimental methods and observations. Scrutiny of the titles immediately reveals the shortcomings of the translation. The titles do, however, indicate to English readers the kind of research in pneumoconiosis which is currently being pursued in Japan. It is hoped that the practice of providing abstracts or summaries in English will be continued.]

A. Meiklejohn

Lippmann, M., Christofano, E. E. & Graveson, R. T. **Lightweight Air-Sampling Pumps for Field Use.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 212–16, 7 figs.

Ann. des Mines. 1958, July, No. 7, 429–36, numerous figs. Prévention de la silicose professionnelle. Masques respiratoires anti-poussières. [**Prevention of Silicosis—Dust Masks**]

In dusty occupations it is not always possible to suppress or remove all the noxious dust in the atmosphere. Accordingly to protect the workman recourse must be had to the use of masks or respirators. It is necessary that these should be of proved efficiency and comfortable in use. At the Government Chemical Laboratory at Bouchet, France, 16 patterns of mask marketed by 13 manufacturers have recently been examined and tested scientifically. At the outset the tests were made with methylene blue, later replaced by indigo vapour and with fine sand. Among the matters investigated were the filtering efficiency, before and after use, resistance to air flow at 1,800 litres/hour, ease of adjustment, stability on the face, comfort in wear and effect on visibility. A description of each mask, name of manufacturer, and results of the various tests are tabulated, and there are several photographs and drawings.

[Of the masks examined the Draeger is the only one in fairly general use in Great Britain. It should be emphasized that in Great Britain the only masks recognized officially for use in factories and mines are those designated "Approved" by the Factory Department and Ministry of Power. This particular matter is of absolute importance in actions for damages at Common Law.]

A. Meiklejohn

Lotta C. La Tubercolosi. 1959, Jan.–Feb., v. 29, Nos. 1/2, 5–68. Il XIV Congresso Italiano di Tisiologia, Cagliari, 26–28 ottobre 1958. [**Fourteenth Italian Congress on Phthisiology, Cagliari, October 1958**]

The 14th Italian Congress of Phthisiology was held in October 1958 at Cagliari, Sardinia, and the inaugural

ceremony coincided with the opening of the very latest preventorium built at Iglesias near Cagliari by the INPS (National Social Insurance Board).

S. Cara, Assessor of Hygiene and Sanitation of the United Sardinian Region, opening the congress, gave an interesting review of the history of tuberculosis in Sardinia, and stated that now, as regards tuberculosis prevention 15,000 children had been examined by X-ray and 12,000 kindergarten and elementary schoolchildren tested by the plaster test. 9·4% were positive to this, and 4·3% were affected with either active or inactive disease. A campaign against bovine tuberculosis was being carried out with slaughter of reactors.

A. Corsi, President of the INPS, mentioned that compared with the rest of Italy tuberculosis was still in the epidemic phase in Sardinia. For all Italy his Board was responsible for 54 sanatoria, 6 preventoria, and a rehabilitation centre at Milan, while it also helped research at various places, including the C. Forlanini Institute at Rome.

The Minister of Health, Professor V. Monaldi (whose appointment as the first holder of this office is a compliment to all tuberculosis workers), gave some figures illustrating the progress made against the disease in Italy between 1920 and 1957. The mortality per 100,000 for adults had fallen from 140 to 22, and for children aged 1 to 14 years from 29·14 in 1920 to 1·54 in 1955. However, at Naples an investigation in 1957 among schoolchildren showed that while the forms of tuberculosis in the elementary and middle schools were almost all benign, the high schools and youth colleges had a morbidity double that of the younger children and the type of disease was definitely evolutive. At present in Italy the tuberculosis mortality was 3 times higher among non-insured persons, but he announced that the draft of a new law providing for the extension of insurance aid to the non-insured in the event of tuberculosis, had just been signed by the President of the Republic.

The Congress had two main themes; silico-tuberculosis, and chronic cor pulmonale in tuberculosis.

I. *Silico-Tuberculosis*

M. Aresu (pp. 19–23) discussed the relationship between silicosis and tuberculosis, especially as regards the morbid anatomy and clinical manifestations. He considered that the 2 processes remained distinct, but for diagnosis, in addition to the 3 fundamental requirements biopsy by the Vim-Silverman needle might be useful for lesions of the diffuse type. He was doubtful about the use of the 35 × 35 mm. film for such patients who should be put in hospital and studied at length. A. Monaco (pp. 23–26) considered that the cause of pulmonary tuberculosis in silicotics had a biological relationship to age, being slow in older persons but having a rapid evolution in younger persons. Antibiotic treatment of the combined disease had almost completely transformed the situation in Cagliari and prophylaxis with isoniazid had been very successful. V. Lubich (pp. 26–30) dealt with the diagnosis of the superimposition of tuberculosis on silicosis. There are no pathognomonic features but tuberculosis is more likely in patients with a hereditary tendency, and it occurs more easily in advanced silicosis. Radiologically, asymmetry of the lesions is important as the apices (and the bases) are not usually affected in silicosis, and with associated tuberculosis, nodulation often becomes coarse with a confluent tendency. Subcutaneous injections of OT at 6–7-day intervals causes a general reaction if tuberculosis is present, without altering the X-ray picture; the exhibition of iodides is also often helpful. Diagnosis of the combined disease was usually not difficult. S. Valenti (pp. 30–39) spoke on the pathogenetic and clinical aspects, pointing out that though in Italy hundreds of thousands of workers are exposed to risk each year only about 1–3% develop silicosis. He gave some statistics from his Genoa clinic for the last 10 years. Of 268 patients thought to have pure silicosis, 72% were Mantoux positive. In the combined disease the tuberculosis element may be atypical both in form and site. He considered that silicosis occurs in persons with a latent or active tuberculosis infection. M. Negri (pp. 39–40) discussed the evolutive form of tuberculosis in silicosis as seen at Grosseto Sanatorium (Tuscany). [Grosseto is the centre of a large pyrites mining area, the pyrites having a high SiO_2 content.] Observations on 70 miners showed that the disease had a fibrosing tendency with a chronic course, and to explain this he considered that the tuberculosis became implanted in a soil modified structurally by reduction of the vascular bed, destruction of the alveoli, emphysema, and by the patient's age. Because of this tendency to fibrosis he did not advise the use of steroids in treatment.

A. Cherchi, M. Congiu, G. P. Nissardi, M. Lixi and A. Sani (pp. 40–42) dealt with respiratory and circulatory physiology. In the combined disease this is profoundly modified as even at rest the haemoglobin is not fully saturated. Cardiac catheterization on 17 patients with silicosis, and 7 with the combined disease, showed a slight increase in the pulmonary arterial pressure. Electrocardiograms (ECG) in 2,020 patients showed changes referable to the heart in 5·6% with silicosis, and 37·7% with the combined disease. The right heart stands overloading quite well as a rule.

II. *Chronic Cor Pulmonale in Pulmonary Tuberculosis*

A. Blasi (pp. 44–47) mentioned that in autopsies on 4,534 patients with pulmonary tuberculosis at Naples chronic cor pulmonale was found in 544 (11·9%); the numbers in recent years had greatly increased. P. Colantuono (p. 48) discussed the effects on the heart of patients treated by surgical collapse. From 1948, 204 patients had been examined; 133 had a thoracoplasty, and 71 an extrapleural pneumothorax. The heart was affected in a large number. E. Catena and G. Galzerano (pp. 48–49) discussed collapse of the lung and cor pulmonale. Studies at Naples on 93 patients who at death had either a unilateral or bilateral collapse showed that rigid collapse causes a true anatomical resistance in the pulmonary circulation, which is of pathogenetic importance. G. di Maria (pp. 49–54), dealing with the cardio-circulatory apparatus in chronic pulmonary tuberculosis, emphasized that lack of hypertrophy does not mean that tuberculosis has no effect on the heart as serious lesions can exist without any effect on the lesser circulation. Anoxaemia is of special importance but in

his experience of 150 patients, cor pulmonale was rare. The ECG is often characteristic with right axis deviation and diphasic or inverted T in D2, D3, and the thoracic leads. S. Rossi (pp. 54–56) dealt with the ECG in pulmonary tuberculosis. Between 1947 and 1958 the ECG was performed on 10,000 patients (5,680 men and 4,420 women) at the C. Forlanini Institute at Rome. 3,780 had abnormal tracings of some sort, mostly atypical voltage, or changes in S-T and T wave; right axis deviation occurred in 743 and left axis deviation in 403. There is no typical ECG syndrome. M. Castelfranco (pp. 58–59) discussed pathogenetic factors in cor pulmonale. The mechanical insufficiency of the vascular bed is related to the size of the right ventricle; hypoxaemia causes increased pulmonary pressure. G. Pezzuoli (pp. 59–60) spoke on the lesser circulation in pulmonary surgery. Investigation of 53 patients from 1 month to 6 years after pneumonectomy or lobectomy by means of angiopneumography, ECG, and cardiac catheterization showed that surgery did not induce pulmonary hypertension later. E. Sartorelli (pp. 61–62), discussing cor pulmonale, stated that it was a frequent complication of silicosis as demonstrated either post mortem or by study of the haemodynamics of the pulmonary circulation; the other usual methods had not helped in diagnosis. Examination of 28 patients with confluent and massive disease showed cor pulmonale in 82%; the ECG on 115 patients showed right ventricular preponderance in only 9·8%. Cardiac catheterization on 30 patients with silicosis showed pulmonary hypertension in a high percentage though by the usual methods there was only a small number. He concluded that cor pulmonale in silicosis must be connected with the organic alterations in the lesser circulation. P. C. Curti, L. Donno and G. L. Scalfi (pp. 62–68) mentioned that at autopsy on 194 patients with pulmonary tuberculosis, cor pulmonale was present in 22%; catheterization of 70 patients frequently showed pulmonary hypertension without any clinical or ECG signs of affection of the right heart. The addition of tuberculosis even if only slight and localized, greatly aggravates the position. Autopsy on 28 patients showed right hypertrophy in 14. Emphysema is an important factor. Cardiac catheterization on 21 patients with the combined disease showed pulmonary hypertension in 60% at rest and in 95% after work. While there is in such cases a functional deficit of ventilation, and pulmonary hypertension especially after work, anoxaemia is not evident, hence the value of treatment by breathing oxygen is not great.

[From the evidence submitted it would seem that cardiac catheterization is of value in demonstrating pulmonary hypertension in the absence of evident signs. In view of Prof. Monaldi's figures on schoolchildren at Naples, it would be interesting to have details of the BCG vaccination results.] *W. K. Dunscombe*

Nordvik, N. La silicose et l'asbestose prédisposent-elles au cancer pulmonaire? [**Are Silicosis and Asbestosis predisposing Causes of Cancer of the Lung**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1959, Feb., v. 17, No. 2, 85–99, 2 figs. [94 refs.]

A grinder of steel castings who suffered from silicosis developed cancer of the lung which was proved by the detection of malignant cells in the sputum. He claimed compensation on the basis that the combined lesions constituted an occupational disease. This question whether or not malignant disease of the lung should be regarded as causally related to pneumoconiosis and so compensatable is not uncommon nowadays; indeed it is an increasingly frequent problem for compensation medical boards. The crucial difficulty is that primary cancer of the lung is a disease prevalent among all groups of the population, irrespective of their occupations. A particular aspect of the problem is the excessively high incidence of lung cancer among heavy cigarette smokers. In the absence of experimental proof that pneumoconiosis and cancer of the lung are linked aetiologically, recourse must be had to studies of the relative prevalence of lung cancer in separate occupational groups. This statistical approach has been used in many field studies all over the world. A review of these studies is the substance of the present article [the author is to be congratulated on the comprehensive bibliography]. The author does not accept that there is any interrelationship between cancer and silicosis but admits the probability in asbestosis. These conclusions accord generally with present thought and practice in Great Britain. The recent observations of J. C. Wagner on mesothelioma of the pleura among workers at asbestos mines in South Africa [*Proceedings of International Conference of Experts on Pneumoconiosis*, Johannesburg, Feb., 1959—in the press: J. & A. Churchill, London] support the conclusion in asbestosis. There is, however, the reservation that all varieties of asbestos mineral may not be equally carcinogenic. At present chrysotile dust particularly is under suspicion.

[The question in respect of both silicosis and asbestosis should be regarded as open. In recent years the National Union of Iron and Steel Foundry Workers in Great Britain has claimed that there is an excessive incidence of cancer not only of the lung but of other organs among their members (see Turner, H. M. and Grace, H. G., this *Bulletin*, 1938, v. 13, 295).

The number of cases recorded by separate observers cannot always be taken at their face value. Thus in Great Britain Gloyne undertook the pathological investigation of asbestosis cases for several observers and so individual cases are common to several reported series. Nearly 25 years ago the interrelationship of cancer of the lung and asbestosis suggested itself to the reviewer when a husband and wife, certified cases of asbestosis, both died of primary cancer of the lung.]

A. Meiklejohn

Bohlig, H., Jacob, G. & Kallabis, B. Über Morbidität und Pathologie des Asbestlungenkrebses. [**Morbidity and Pathology of Lung Cancer with Asbestosis**] *Ztschr. f. Unfallmed. u. Berufskrankh.* 1959, Mar. 15, v. 52, No. 1, 64–78, 3 figs. [Numerous refs.]

The extensive world literature on cancer of the lung in asbestos workers and on related subjects is here reviewed at considerable length with statistical analysis and critical discussion. From these reports the admittedly rough estimate is made that among 40,000 asbestos workers in the world 80 cases of lung cancer have been

reported in 20 years. The opinions and conclusions of different observers vary considerably and these differences are examined. Particular consideration is given to the importance of skilled autopsy examination and the difficulties which may exist in forming an opinion on whether in a particular case exposure to asbestos contributed to the development of cancer.

Much more research on this cancer problem is needed but up to the present it is stated that a comparison of the expectation of pulmonary cancer in the general population with that of workers in asbestos shows that in the latter groups the risk of cancer is not increased. The morbidity curve of cancer with asbestosis perhaps reaches its peak at a somewhat earlier age than that of non-industrial bronchial carcinoma. *M. E. Delafield*

HIRSCH, M. J., KASS, I., SCHAEFER, W. B. & DENST, J. **Infection with Atypical Tubercle Bacilli in Graphite Pneumoconiosis.** *Arch. Intern. Med.* 1959, May, v. 103, No. 5, 814–7, 2 figs. [11 refs.]

Graphite pneumoconiosis is comparatively rare. In the literature of the subject post-mortem findings have been reported in 7 cases but though pulmonary cavitation occurred in 5 of these, in 1 case only was it attributed to tuberculosis.

A 52-year-old white man while employed at a graphite mine in Texas, where he had worked for 9 years, developed a spontaneous pneumothorax, which was complicated by pleural effusion. Radiographic examination revealed diffuse pulmonary fibrosis, which was diagnosed as graphite pneumoconiosis, and excavating tuberculosis of the right upper lobe. This was treated by lobectomy and the diagnosis of pneumoconiosis was confirmed. The particular interest of the case is in the bacteriological findings. Acid-fast bacilli were cultured from the sputum and directly from the resected pulmonary cavity. On oleic-acid-albumin agar at 37°C. the colonies were round, white and glistening. The colonies, after exposure to daylight, became slightly wrinkled and cream-coloured, but not yellow. They were strongly catalase-positive, rapidly decomposing hydrogen peroxide. The organisms were non-pathogenic for guineapigs, mice, chickens and rabbits. They were, from the outset, completely resistant to 20 μgm. of streptomycin per ml. and to 3 μgm. of isoniazid per ml., partially resistant to 10 μgm. of isoniazid per ml. and susceptible to 2 μgm. of amino-salicylic acid per ml. Organisms with these characteristics have been classified with those of the non-photochromogenic "Battey" type. [The symbol "γg." is used throughout for these quantities of drugs per ml., but evidently refers to microgrammes (μgm.).]

In the present case the organism is regarded as an atypical nonchromogenic mycobacterium and the pneumoconiosis is considered to be a factor predisposing to progressive infection with organisms which are not ordinarily pathogenic for man. A few similar cases have been reported in association with silicosis.

A. Meiklejohn

i. TILLER, J. R. **An Investigation of Byssinosis in a Rayon Mill.** *Trans. Ass. Indust. Med. Officers.* 1958, Jan., v. 7, No. 4, 157–60.

ii. —— & SCHILLING, R. S. F. **Respiratory Function during the Day in Rayon Workers—a Study in Byssinosis.** *Ibid.*, 161–2.

i. Byssinosis has been reported in men and women exposed to cotton, flax and hemp. It has not been reported in those working with man-made fibres, though some of these contain cellulose, and are worked in the same manner as cotton.

In a mill that had been spinning viscose rayon for 20 years, 91 out of a total of 93 card-room and blow-room workers were interviewed and asked similar questions to those asked in other byssinosis prevalence surveys.

No byssinosis was found among those who had only been exposed to rayon. Of the 73 workers who had also been exposed to cotton dust previously, 15 had had byssinosis. Since working in rayon these 15 have lost their regular chest tightness on Mondays (first day of work after absence). 6 are symptom-free, the others having residual bronchitic symptoms.

ii. The clinical findings in this mill were confirmed by ventilatory function tests on those who had had byssinosis and matched controls. The maximum breathing capacity was measured (by the indirect method) before and after work on a Monday. There was no significant change in ventilatory capacity during the day in this group. This contrasts with a mean fall in ventilatory capacity of 14% in byssinotics and 6% in normal subjects in those working in cotton card rooms.

Both these clinical and physiological findings indicate that the causative agent of byssinosis is absent in a rayon mill. *C. H. Wood*

STOTT, H. **Pulmonary Disease Amongst Sisal Workers.** *Brit. J. Indust. Med.* 1958, Jan., v. 15, No. 1, 23 37, 5 figs. [22 refs.]

"A study was made in Kenya in a factory making ropes and bags from sisal to determine whether the dust produced causes pneumoconiosis or other chest diseases.

"The average dust concentration in the card rooms was 243 particles per ml. (0·5 to 5 μ). Other parts of the factory were relatively dust free. Deposited dust had a very low silica content.

"The respiratory illness sickness rate was twice as high in the card-room workers as in those working in other parts of the factory.

"Radiographs of 37 workers with between six months' and 15 years' exposure in the card rooms revealed four with a similar type of apical fibrosis. Two showed heavy lung markings. In 46 films of workers of long experience in other parts of the factory only one showed heavy lung markings and none apical fibrosis.

"The average maximum breathing capacity (recorded for one minute) was 53 l./min. in 36 card-room workers and 61 l./min. in 25 workers in other parts of the factory and of similar age. The difference is statistically significant.

"No worker exposed to sisal dust gave the characteristic history of byssinosis. Skin sensitivity tests with extracts of sisal were uninformative.

"A subsidiary radiological survey of men in three sisal estates showed no evidence of pneumoconiosis or apical fibrosis but the exposure of the workers had been short and the dust concentration low.

"The apical fibrosis is unlike that seen in the general African population. Intensive investigations for tubercle bacilli were negative.

"It seems possible that the fibrosis is related to occupation; its possible relation to the chest disease occurring in workers in bagasse and peppers is discussed."

SCHEPERS, G. W. H. **The Pulmonary Reaction to Sheet Fiberglas-Plastic Dust.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 73–81, 7 figs.

The use of Fiberglas plastics in industry is relatively new but increasing. Workmen employed in the manufacture of these materials and in such operations as sawing, sanding and burnishing in the fabrication of motor car bodies are exposed to the inhalation of very high concentrations of fine dust in the course of their employment. Although adverse pulmonary effects have not so far been observed, responsible employers have taken precautions to minimize any possible risk. In 1958 Schepers and his colleagues at the Saranac Laboratory, New York [this *Bulletin*, 1959, v. 34, 57] reported the results of animal experiments in which they used samples of dust obtained from actual processes. The material was a moulded Fiberglas plastic incorporating pulverized calcium carbonate as a filler. The study of the biological effects of this material on rats, guineapigs and rabbits suggested that it may be classified in the group of inert dusts. A parallel experiment, not absolutely identical in detail, was conducted with dust of sheet Fiberglas-plastic in which pulverized calcium sulphate is the filler. Comparison of the results of the 2 studies indicated that substitution of calcium sulphate as a filler may decrease the biological responses to inhaled dust of sheet Fiberglas-plastic. *A. Meiklejohn*

DESOILLE, H., HADENGUE, A. & FELETIN, R. Troubles respiratoires provoqués par la gomme arabique. [**Respiratory Distress induced by Gum Arabic**] *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 282–3.

This is an account of a printing worker, aged 42, who developed asthmatic attacks, severe enough to need a bronchorelaxant, each afternoon while working, but not when away from work. He had worked in the same place since 1929, and his symptoms began after gum spraying was introduced 2–3 years ago. There was no past or family history of asthma. There were some adventitious sounds in the lung, but otherwise clinical examination and blood counts were normal. X-ray examination of the chest showed normal translucency with slightly accentuated hilar shadows. Patch tests with gum arabic solution and workroom dust were negative.

Respiratory function was measured before and after inhaling an aerosol of gum arabic in water and alcohol for 2 minutes. Though the subject experienced no dyspnoea during the experimental conditions, there was an unquestionable decrease of vital capacity which persisted and was subsequently accentuated after inhaling an aerosol of aminophylline. The experimental conditions did not approach in severity the atmospheric conditions of the workroom where towards the end of the day the atmosphere was genuinely misty from the spray which on drying gave rise to much dust.

M. Patricia Fitzsimons

FLEISCH, A. Le "Métabographe": Appareil pour l'enregistrement direct chez l'homme de la consommation d'oxygène, de la production de gaz carbonique, de l'amplitude respiratoire, du débit et de l'équivalent ventilatoires et du quotient respiratoire. [**The Metabograph, an Apparatus for Direct Measurement in Man of Oxygen Consumption, Production of Carbon Dioxide, Tidal Volume, Minute Volume, Ventilatory Equivalent and Respiratory Quotient**] *Helvetica Physiol. & Pharmacol. Acta.* 1953, v. 11, No. 4, 361–94, 9 figs. [22 refs.]

The metabograph is an ingenious but complicated closed-circuit apparatus for measuring human metabolism in the basal state and also at work rates up to oxygen consumption of 5 litres per minute. The following factors are simultaneously recorded:—tidal volume, minute volume, oxygen consumption and carbon dioxide production, the ventilatory equivalent for oxygen and the respiratory quotient. The vital capacity with its subdivisions and the maximum breathing capacity can also be determined.

The instrument has no stopcock or valves and has a low respiratory resistance. The author describes the apparatus in detail and gives sample traces showing the effect of voluntary hyper-ventilation, alterations of tension of inspired oxygen and 2 grades of work on a bicycle ergometer. *M. L. Thomson*

HARADA, K. **Changes in Pulmonary Compliance before and after Lung Resection and Relations between Dynamics of Pulmonary Circulation and Pulmonary Compliance.** *Tokushima J. Exper. Med.* 1959, Feb., v. 5, No. 4, 377–89, 8 figs. [41 refs.]

DINISCHIOTU, G. T., RĂDULESCU, I. C., PREDA, N. & GEORGESCU, A. M. Die klinischen Kategorien des industriellen Saturnismus. [**Clinical Categories of Industrial Lead Poisoning**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 2, 127–47, 1 fig. [33 refs.]

The authors of this paper express the opinion that although much excellent work on the aetiology, clinical aspects, prophylaxis and treatment of lead poisoning has been carried out, the pathophysiological process in relation to the clinical picture has not been sufficiently studied. Accordingly, in this paper there are described observations and investigations, based on an experience of several hundred cases of lead poisoning, which are divided into 3 groups:—(1) the main and subsidiary aetiological factors in lead poisoning, (2) individual reactions to lead and their associated problems and (3) the development of lead poisoning in special relation to the time factor. In these 3 sections the subject matter is described and discussed in some detail and references are given to much published work.

It is suggested that types of lead poisoning might be classified into certain categories after study of the symptomatology, the changes in the findings of laboratory investigations during the course of the illness and the history of the patient. These proposed categories of lead poisoning which are fully described are:—(1) progressive or evolving, (2) non-progressive, (3) asymptomatic, (4) suspected, (5) acute and (6) progressive with acute manifestations.

M. E. Delafield

DINISCHIOTU, G. T., RĂDULESCU, I. C. & MUICĂ, N. Hämodynamische Studien in der industriellen Bleikrankheit. [**Haemo-dynamic Studies in Industrial Lead Poisoning**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 2, 148–67, 3 figs. [Numerous refs.]

This is a long paper in which description, tables and figures record in considerable detail the results of the laboratory examination of 20 men with chronic lead poisoning, 12 with lead colic and 7 men who had had lead colic a considerable time before. The examination consisted of applying the physical and physiological method (WEZLER-BÖGER method, *Ergebn. Physiol*, 1939, v. 41, 292) of making a number of measurements of the heart and circulation—heart volume, blood pressures, stroke volume, peripheral resistance, cardiac work performed and others.

The findings of this elaborate investigation were that, adopting the normal standards according to Wezler and Böger, no important deviation of the measurements were manifest in the men with chronic lead poisoning. During lead colic there is a marked increase in resistance in the peripheral circulation and in the period which follows lead colic there is present a disturbance of the regulation of the blood dynamic system and a tendency to hypotonia which last for a considerable time. These disturbances are attributed to the action of lead on the vegetative nervous system.

M. E. Delafield

TADA, O. [**On the Lead Content of the Whole Blood.**] *J. Sci. of Labour.* Tokyo. 1959, May, v. 35, No. 5, 401–9, 5 figs. [10 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

i. "With an intention to establish a precise method of determining blood lead content, the normal levels in the whole blood were investigated for lead, bismuth, copper, zinc and iron which are considered to interfere with the lead analysis.

"Variations of content of the five metals in the whole blood were observed for a month on eleven healthy men working in the institute. The difference by age in content of the metals in the whole blood was also studied comparing five men in the twenties and five men in the forties, and the bismuth concentration in the whole blood was determined in a person before and after oral administration of 3 g of bismuth subcarbonate daily for three days.

"Results: (1) The content of each metal in the whole blood was rather constant, and the difference by age was indistinct (Fig. 1 and 2). The average content of each metal in eleven healthy men was found to be: lead, 14 ± 5γ/100 g; bismuth, 0–4γ/100 g; copper, 105 ± 25γ/100 g; zinc, 570 ± 40γ/100 g; iron, 48.5 ± 2.5 mg/100 g.

"(2) From the data of 33 office and laboratory workers, including the above mentioned subjects, without the exposure to lead, the normal range of blood lead content was regarded as 2–30γ/100 g (15γ/100 g in average) and 60.6% of all the persons fell in the range of 11–20γ/100 g (Table 1).

"(3) The bismuth content of the whole blood was very low and was found in the range of 0–2γ/100 g except a case of 4γ/100 g. It was increased in a person by oral administration of bismuth subcarbonate, but the maximum level observed was 4γ/100 g (Fig. 3).

ii. "Determinations of blood lead content of workers and atmospheric lead concentration had been carried out in various workshops in twelve years from 1947 to 1958. The results of determinations are shown in Fig. 4 and 5. The percentage distribution of blood lead content is shown in Table 1 according to the kind of work.

"(1) The operations yielding lead dust raise remarkably the atmospheric lead concentration in the workshops. On the other hand, the operations generating lead fumes seem to be liable to raise the blood lead content of workers even while the atmospheric lead concentration is not so high.

"(2) Among 656 workers exposed to lead dust or fume, the blood lead content was higher than 30γ/100 g in 35.9% of them, and higher than 60γ/100 g in 6.3%. The difference between them and workers without exposure to lead was quite remarkable."

MIKI, M. **Studies on the Lead Content in the Bodies of Test Animals. I. Lead in Blood, Urine and Feces of the Rabbits.** *Osaka City Med. J.* 1958, Jan., v. 4, No. 2, 135–48, 21 figs.

"The content of lead in blood, urine and feces of the healthy, male adult rabbits has been measured by the spectrochemical analysis method which was contrived by the author, in order to clarify its distribution. Several statistical laws have been found as the result:

"1) The distribution of the lead amount in the whole blood of the rabbits approximately follows the distribution of a logarithmic normal type, its mean value (μ) being 34.6 mcg/100 gm, and the upper limit is 104.4 mcg/100 gm at the one-side significant level of 5%.

"2) The distribution of lead in the urine of the rabbits approximately follows the distribution of a logarithmic normal type, the mean value (μ) being 21.13 mcg/100 gm, and the upper limit is 66.8 mcg/100 gm at the one-side significant level of 5%.

"3) The distribution of lead in the feces of the rabbits approximately follows a normal distribution type, the mean value ($\bar{\chi}$) being 163.66 mcg/10 gm, and the upper limit is 268.5 mcg/10 gm at the one-side significant level of 5%.

"These representative values and their upper limits, being obtained from about 300–400 of healthy, male adult rabbits, may be applicable to a larger population, since each measured value follows statistical laws of distribution."

TEISINGER, J. & SRBOVÁ, J. **The Value of Mobilization of Lead by Calcium Ethylene-Diamine-Tetra-Acetate in the Diagnosis of Lead Poisoning.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 148–52, 3 figs. [17 refs.]

The published data relating to normal lead content in human urine show considerable differences. Different living conditions, food supplies, different lead content in soil and vegetables, and in the water supply, must be taken into consideration. The authors consider, from their experience, that in Czechoslovakia an amount of 0·100 mgm. of lead in 24-hour urine is the highest normal value. On an average, however, the values are much lower, *i.e.*, 0·031 to 0·043 mgm./24 hours. The laboratory tests at present employed for the diagnosis of lead poisoning fail where exposure is not very severe and particularly when a considerable time has elapsed since termination of exposure. The work described in the present paper was undertaken to measure the urinary lead excretion after administering $CaNa_2EDTA$ to normal and lead-exposed subjects, and to attempt to relate the amount of urinary lead excreted to the diagnosis of lead poisoning.

Each individual was given a single intravenous injection of 15 ml. of a 20% solution of $CaNa_2EDTA$ (2·8 gm. of anhydrous substance). In a control group of 50 individuals who had never worked with lead it was found that, after injection, the amount of urinary excreted lead rose considerably, but did not exceed 0·350 mgm./24 hours. In a group of 47 who had formerly worked with lead or who were still engaged in this work but did not show any symptoms of poisoning, the urinary lead levels before injection were higher than in the control group. Their average value was within the confidence limits of $0{\cdot}067 < \chi < 0{\cdot}082$ mgm./24 hours with probability of 99%, the extreme values obtained being 0·012 and 0·268 mgm./24 hours. After injection, the average in this group lay with a probability of 99% within the confidence limits of $0{\cdot}612 < \chi < 0{\cdot}629$ mgm./24 hours, the extreme values being 0·166 and 3·212 mgm./24 hours.

In 10 severe cases of lead poisoning (as evidenced by anaemia, colic, severe subjective symptoms, and high values in laboratory tests) it was found that, after an injection of $CaNa_2EDTA$, lead excretion was increased to values from 6·2 to 15·2 mgm./24 hours. In a group of 10 slight, or "laboratory" cases of poisoning (showing a fall in haemoglobin), urinary lead values varying around 2·5 mgm./24 hours were found after the injection.

Examination of the urine of 10 unexposed individuals, undertaken at intervals of 3 hours, showed after injection of $CaNa_2EDTA$ no higher lead concentration than 0·500 mgm./litre, the highest concentrations being observed 6 hours after injection. In the urine of individuals exposed to lead or suffering from lead poisoning a higher urinary lead concentration was found than in the control group, and in these cases the maximum was found at various time intervals.

After a discussion of their results in relation to work of a similar nature carried out by other observers the authors conclude that the mobilization of lead may be of considerable value in the diagnosis of atypical cases of chronic lead poisoning, but the results can be evaluated only in association with the general clinical picture. *P. J. R. Challen*

GLÖMME, J. & GUSTAVSON, K. H. **Treatment of Experimental Acute Mercury Poisoning by Chelating Agents BAL and EDTA.** *Acta Med. Scandinavica.* 1959, June 6, v. 164, No. 2, 175–82, 4 figs. on 2 pls. [11 refs.]

Rats were poisoned in 3 ways, with mortality rates between 70% and 90%: by subcutaneous injection of 10 mgm./kgm. $HgCl_2$ in 1 ml. saline, by intragastric administration of 70 mgm./kgm. $HgCl_2$ and by intraperitoneal injection of 12 mgm./kgm. methylmercuric-dicyandiamide. At various times afterwards some groups were treated with BAL (2:3 dimercaptopropanol) or EDTA (the calcium di-sodium salt of ethylenediamine-tetra-acetic acid) intraperitoneally and others, the controls, were given saline injections at the same times. In poisoning by the organic mercurial BAL had no significant beneficial effect; EDTA resulted in higher mortality rates in rats injected with $HgCl_2$, than in controls, but BAL reduced the rates in both forms of corrosive sublimate poisoning, particularly well when given repeatedly during the first day and when started within 2 hours of parenteral or 12 hours of peroral administration.

When 13·3 mgm./kgm. BAL was injected 3 times daily for 3 days, starting either 1, 6 or 12 hours after peroral $HgCl_2$, the 14-day mortality rates were 0%, 30% and 50% (controls 73%). When 10 mgm./kgm. BAL was injected 4 times daily for 3 days, starting either ½, 2, 4 or 6 hours after parenteral $HgCl_2$, the rates were 7%, 0%, 41%, and 90% (controls 88%); with 1 dose only of 20 mgm./kgm. BAL, starting at these same times, the rates were 20%, 33%, 67% and 88% (controls 89%). In smaller groups, starting 4 hours after parenteral $HgCl_2$, BAL in varying doses, namely 20 mgm./kgm. once, or 10 mgm./kgm. 4 times for 1 day or 4 times daily for 3 days, gave rates of 75%, 31% and 46% (controls 92%): results were approximately the same when therapy was discontinued after 1 day as when continued for 3.

On the other hand, when 125 mgm./kgm. EDTA was injected ½ hour after parenteral $HgCl_2$ and repeated 4 times daily for 3 days, 3 of 22 rats died on the 1st day, 9 on the second, 6 on the 3rd, 3 on the 4th and 1 on the 5th (controls 1, 3, 9, 6 and 0, 2 of the 22 being alive after 14 days).

The degree of renal cortical damage in the rats injected with $HgCl_2$ and treated with BAL or EDTA was in accordance with the mortality rates. The severity of the lesions was assessed in 4 grades, ranging from swelling of tubular epithelium to complete necrosis and then a semi-quantitative evaluation was made of the relative areas of the longitudinal section occupied by each of the 4 grades. *M. Patricia Fitzsimons*

BONNELL, J. A., KAZANTZIS, G. & KING, E. A. **Follow-Up Study of Men exposed to Cadmium Oxide Fume.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 135–47, 3 figs. [19 refs.]

In 1953 the health of 100 men exposed to cadmium fume during the manufacture of copper-cadmium alloys at two factories in England was investigated [this *Bulletin*, 1956, v. 31, 295]. As a result of that survey 19 cases of chronic cadmium poisoning were described among the men then at work, and 4 men who were so disabled by their symptoms as to be unable to work were examined in hospital, making a total of 23 cases. Of these 23 men, 11 had emphysema and proteinuria, 8 had proteinuria alone, and 4 had emphysema alone. One man died in uraemia, the result of chronic renal failure. Because of reports of further cases of proteinuria at one of these factories the authors undertook a follow-up study of the exposed men in 1957, 4 years after the original survey. It was hoped to obtain information about the course of the disease, particularly on whether it was self-limiting in the absence of further exposure to cadmium, and whether the first symptoms or signs of poisoning could occur after a latent interval. [This is an extremely interesting and thorough investigation and those readers who are interested in the toxicity of cadmium should read the original.]

83 of the 100 men were re-examined, and in all, 24 new cases of chronic cadmium poisoning were discovered, 5 with emphysema and proteinuria, 1 with emphysema alone, and 18 with proteinuria alone. It is clear that the first sign of chronic cadmium poisoning can occur after a long latent interval following cessation of exposure to cadmium for 6 of the 10 new cases in one factory had no exposure after 1950 and in the other factory 4 of the 14 new cases had their last exposure in 1953.

The result of atmospheric sampling suggest that working conditions have improved since the earlier survey, and therefore it is unlikely that any of the 24 new cases were due to absorption of cadmium in the period 1953 to 1957. The men diagnosed as having chronic cadmium poisoning in 1953 showed evidence of deterioration and this was confirmed by respiratory function tests when due allowance was made for ageing from a comparison with a control group.

Cadmium workers have an increased amino-acid content of the urine (CLARKSON and KENCH, *Biochem. J.*, 1956, v. 62, 361), and, in the absence of hepatic failure, this is a manifestation of renal tubular damage. The amino-aciduria is more severe in those persons excreting the specific cadmium protein. During this survey it was found by means of a sensitive qualitative test for glucose that 19 of the 82 men had glycosuria. Together with the post-mortem findings in one case, abnormal renal function tests in 3 other cases and the evidence from animal experimentation, the above facts would suggest that progressive renal damage does occur after prolonged absorption cadmium.

The measurement of cadmium of face masks worn for a single operation by men employed at one factory showed that even under the improved working conditions large amounts of cadmium could have been absorbed by a careless workman and suggested that the ventilation system could be improved further.

[As the average workman is none too meticulous concerning his own health and safety at work, the results of this latter study suggest that it is feasible that some of the 24 new cases may have been due to continued absorption during the period 1953 to 1957.]

P. J. R. Challen

WALKLEY, Janet. **A Study of the Morin Method for the Determination of Beryllium in Air Samples.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 241–5. [20 refs.]

"A method is presented for the fluorimetric determination of beryllium with morin which is sensitive to 0.004 μg of Be in an aliquot or 0.02 μg per sample. With 0.01 μg Be in an aliquot there is no interference from 100 μg of Ca, Cu, F, Fe, Mg, PO_4, Ti, U, and Zr. At a concentration of 100 μg, Zn gives a fluorescence equivalent to 0.004 μg of Be, but does not interfere at a level of 75 μg. The method has been successfully applied to air samples on ashless filter paper, glass fiber filters, M.S.A. type S pleated filters, and molecular type filters. Directions are given for the preparation of these samples. Recoveries of Be from spiked samples show that the method is satisfactory for the tolerances and ranges encountered in air sampling procedures, and results of typical field samples are shown."

[See this *Bulletin*, 1953, v. 28, 438.]

GADRAT, J., QUERCY, J. & FEDOU. Hémopathie atypique consécutive à une intoxication benzolique chronique. **[Atypical Blood Changes following Chronic Benzene Poisoning]** *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 295–7.

This fairly detailed account of a patient, aged about 57, who had been investigated in 1954 for eczema and gastritis, includes full blood counts. In 1954 there was a slight relative mononucleosis, other examinations were normal and a diagnosis was made of benzene poisoning. The patient had used rubber solvents in his work for 3 months without protection. The total white cell count was 8,000 per cmm., later 7,000; the red cell count was 5,300,000 per cmm. and later 4,700,000.

In December 1957 he was admitted to hospital again for a widespread irritating rash and continuing digestive upset, and was found to have leucopenia, 1,000 white cells with a normal differential count and a corresponding sternal count. The red cells were 4,100,000. Platelets and bleeding time were normal. In January a relative eosinophilia developed and the white cells dropped to 600. Blood transfusions, corticotherapy and vitamin B6 produced no change in the blood. In February cellulitis of the arm with lymphangitis, axillary adenitis and pustular lesions on neck and trunk made the patient gravely ill. The white cells then numbered 800 of which 48 were polymorphs and 36 eosinophils. Pharyngeal examination and numerous blood cultures were negative.

Multiple antibiotics and local treatment to the arm were followed in 3 days by general improvement and

localization of an abscess in the arm from which pus was released which grew a staphylococcus. The condition settled in 6 days. The infection seemed to have given rise to a slight granulocytic reaction, the white cells rising to 1,200. The blood picture then remained the same despite transfusions, vitamin B6 and nucleotide.

M. Patricia Fitzsimons

GILDENSKIOLD, R. S. **[Maximum Permissible Concentration of Carbon Bisulphide in the Atmospheric Air of Residential Districts]** *Gigiena i Sanitariya.* Moscow. 1959, v. 24, No. 6, 3–8, 2 charts. [In Russian.]

The English summary appended to the paper is as follows:—

"The field experience with the previously accepted maximum permissible concentrations of carbon bisulphide in the atmospheric air (the maximum concentration at one time—0.5 mg/m³; the daily average concentration—0.15 mg/m³) has shown that these values were too excessive. These standards have been checked experimentally and new maximum permissible concentrations of carbon bisulphide have been established on hygienic bases. The threshold value of smell sensation for carbon bisulphide in the most sensitive persons comprises 0.05 mg/m³. The reflex action by the method of optic chronaxy and adaptation to darkness, has been obtained with threshold values of 0.04 mg/m³. The subthreshold concentration was 0.03 mg/m³. On the basis of these investigations the authors recommend to accept 0.03 mg/m³ as the maximum permissible concentration of carbon bisulphide in the atmospheric air. The examination of the atmospheric air in the vicinity of an artificial viscose fiber plant, devoid of any air purifying installations, has shown the air to be heavily polluted with carbon bisulphide within the radius of 1000 m (0.04 mg/m³) with the spreading of gas to a distance of 3000 m (0.03 mg/m³)."

LEVINSKAS, G. J. & PASLIAN, Marian R. **Decaborane Effects upon Yeast Metabolism.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 230–34, 4 figs. [12 refs.]

It is difficult to study the mechanism of action of decaborane on isolated systems because it is only sparingly soluble in water and other solvents which would not themselves injure tissues or enzyme systems. It is possible to do so, however, with yeast cells as the test system.

"Yeast cells, suspended in buffered solutions to which decaborane had been added, were shaken overnight in a Dubnoff shaker at 30°C. The following morning, the cells were centrifuged and the supernatant solutions were discarded. The yeast cells were then washed three times with distilled water and aliquots of the washed cells were taken for the respiration studies which were conducted with a Warburg respirometer. Buffered phosphate solutions (*p*H 4.8–5.2) were employed for the prior incubation and the subsequent study of respiration. In the fermentation studies, bicarbonate buffered solutions (*p*H 5.7–6.2) were similarly used.

"Decaborane was found to be inhibitory to the respiration and the fermentation of yeast cells when glucose was employed as the substrate. In addition, the respiration of the decaborane-treated cells was markedly reduced in the presence of other substrates such as pyruvic acid, lactic acid, ethyl alcohol and glycerine. By contrast, the metabolism of ascorbic acid was not markedly affected under similar conditions.

"The yeast/decaborane ratios of the incubated solutions were found to affect the results. If two different yeast concentrations were exposed to the same molarity of decaborane, the inhibitory effect was more pronounced on the dilute yeast solution. By contrast, the effect of pyridineborane, which also inhibits the respiration, is independent of the yeast/borane ratio."

FRISTEDT, B. I. & OHLSSON, W. T. L. Förgiftningsfaror vid användning av organiska fosforföreningar. **[Toxic Risks of the Use of Organic Phosphates]** *Nordisk Med.* 1959, May 28, v. 61, No. 22, 826–8. [30 refs.]

The English summary appended to the paper is as follows:—

"The extensive use of organic phosphates, especially the alkyl phosphates, involves an increasingly severe risk of poisoning, sometimes with a lethal outcome. In most cases there is no lasting damage and the victim will recover completely, but some instances of residual muscular paralysis have been reported.

"The problem is discussed in connection with a case of paralysis in the extremeties, following acute poisoning with parathion."

BERRY, W. K., DAVIES, D. R. & GREEN, A. L. **Oximes of $\alpha\omega$-Diquaternary Alkane Salts as Antidotes to Organophosphate Anticholinesterases.** *Brit. J. Pharmacol. & Chemotherapy.* 1959, June, v. 14, No. 2, 186–91, 2 figs. [15 refs.]

"Sixteen compounds of the general structure $\{HON:CH.C_5H_4N+[CH_2]_n.R+\}2Br$ have been synthesized, in which the position of the oxime group in the pyridine ring, the second charged group R +, and the number of methylene groups between the charged atoms have been varied. The rate at which these compounds reactivate cholinesterase inhibited by ethyl pyrophosphate has been studied and a number have been found which are more active than 2-hydroxyiminomethyl-*N*-methylpyridinium methanesulphonate. Since considerable variation in structure was found among those compounds which are better reactivators than the latter, the concept that 2-hydroxyiminomethyl-*N*-methylpyridinium salts are unique in their ability to fit the surface of the inhibited enzyme is no longer tenable. The reactivating power of these oximes correlated well with their ability, when in conjunction with atropine, to save the lives of mice poisoned by ethyl pyrophosphate. The most effective compounds, *NN'*-trimethylenebis-(4-hydroxyiminomethylpyridinium bromide) and *NN'*-hexamethylenebis(2-hydroxyiminomethylpyridinium bromide), contained a further oxime group in R +, but the second oxime group was not essential for high activity. These new oximes were also superior in saving the lives of

mice poisoned with sarin (isopropyl methylphosphonofluoridate), but the improvement was not as dramatic as when the mice were poisoned with ethyl pyrophosphate. The toxicity of the compounds varied with both *n* and R + and was unrelated to the therapeutic potency."

HOBBIGER, F. & SADLER, P. W. **Protection against Lethal Organophosphate Poisoning by Quaternary Pyridine Aldoximes.** *Brit. J. Pharmacol. & Chemotherapy.* 1959, June, v. 14, No. 2, 192–201. [40 refs.]

"The effect of 18 pyridinium aldoximes on diethylphosphoryl-acetocholinesterase *in vitro* and the protection against lethal poisoning by ethyl poisoning by ethyl pyrophosphate (TEPP) in mice pretreated with 0.095 m.mole/kg. of these oximes was investigated. Monoximes and dioximes of polymethylenebispyridinium compounds were studied in greater detail since they were up to 22 times more potent than pyridine-2-aldoxime methiodide (2-hydroxyiminomethyl-*N*-methylpyridinium iodide) in reactivating diethylphosphoryl-acetocholinesterase *in vitro* and protected mice against lethal poisoning by up to 15 LD100 of ethyl pyrophosphate. These oximes were also up to 52 times more potent than pyridine-2-aldoxide methiodide in reactivating di-isopropylphosphoryl-acetochlinesterase *in vitro* and were effective in preventing lethal poisoning by dyflos (di-isopropyl phosphorofluoridate). The antidotal action against diethyl phosphostigmine (Ro 3-0340) was even greater than that against ethyl pyrophosphate. Some of the most effective oximes had antidotal actions in poisoning by ethyl pyrophosphate, diethyl phosphostigmine and dyflos when given in 0.0095 m.mole/kg. and this effect was enhanced by 1 mg./kg. atropine sulphate. *In vivo* reactivation of diethylphosphoryl-acetocholinesterases by 0.0095 or 0.095 m.mole/kg. of oximes of polymethylenebispyridinium compounds was demonstrated in blood but not in brain. Atropine-like and neuromuscular blocking activities were studied on isolated organs and protection against lethal doses of neostigmine and related anticholinesterases were also investigated. Some of the oximes of polymethylenebispyridinium compounds have, relative to pyridine-2-aldoxime methiodide, a higher therapeutic ratio in mice and considerably greater water-solubility. The possible advantages to be gained from their use in preference to pyridine-2-aldoxime methiodide are discussed."

MINISTRY OF HEALTH. DEPARTMENT OF HEALTH FOR SCOTLAND. **Radiological Hazards to Patients. Interim Report of the Committee** [ADRIAN (Chairman)]. 22 pp., 1 chart. 1959. London: H.M. Stationery Office. [1s. 3d.]

The terms of reference were: "To review the present practice in diagnostic radiology and the use of radiotherapy in non-malignant conditions, having regard to the report of the Committee on the Hazards to Man of Nuclear and Allied Radiations [this *Bulletin*, 1956, v. 31, 1054] and to make recommendations".

The Committee set itself a two-fold task: (1) a nation-wide survey of radiological procedures to estimate the present level to which the population is exposed, (2) to consider the particular diagnostic and therapeutic procedures in present use, with the object of eliminating all unnecessary radiation of the gonads and of the body generally.

Although all the subjects under (1) have not yet been finally surveyed, one of them has, *viz.* the use of X-rays in mass miniature radiography. This is in fact the main subject of the Interim Report and reference is made to the fact that the hazards of ionizing radiation have been widely publicized, with the consequence that there is a danger that X-ray diagnosis and therapy of every kind will be viewed with unnecessary suspicion by the public at large.

In 1957 a total of 3,451,060 mass miniature radiographic examinations were made in England and Wales, the number being 1,319,867 for Scotland. For the whole of Britain there were thus discovered 17,835 cases of pulmonary tuberculosis. Over 63,000 other abnormalities were detected and these included 2,362 cases of lung cancer, nearly 12,000 cardiac abnormalities and 9,400 cases of pneumoconiosis.

The survey has included a very large number of measurements made of the dose received by patients under the varied circumstances of different types of radiological examination. They comprise some 5,000 examinations in 140 hospitals and chest clinics chosen to give a representative selection of radiological work throughout all the 19 hospital regions of Great Britain.

In a final summary it is stated that "On the principle that all unnecessary exposures should be prevented, the Committee endorse the steps already recommended to reduce even the present small dose and further recommend that mass miniature radiography should not be used as a case-finding procedure in children or in pregnant women." Elsewhere it is stated that the value of diagnostic radiography is so great that "there is no doubt that much individual suffering would follow any unnecessary curtailment of those services": and that these examinations when properly conducted make a negligible contribution to the total radiation to which the population is exposed. *S. Russ*

BAIER, E. J. **Radiation — a Photofluorographic Study.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 113–17, 1 fig. [11 refs.]

This article from the Pennsylvania Department of Health is the result of an attempt at evaluating the radiation exposure of the general public when submitted to X-ray fluoroscopy. This does not mean that it represents a national survey in any sense of the term. Technically it has considerable interest. For gonadal region exposure, two dosimeters were tied to a stout cord which was used as a belt on the patient, one dosimeter on the front the other on the back. For area monitoring, tests were carried out in the vicinity of the patient being irradiated. Staff clerks were found sometimes to be located in an appreciably irradiated region; this was easily remedied. An unlooked for finding occurred in the group of people in the waiting line ready to be X-rayed (mass radiography). These people are near the X-ray plant and received radiation therefrom. An example may be given: A 0·200 milliroentgen

dosimeter was placed in the shirt pocket of one of the subjects. As he approached the unit, his cumulative dose was determined and it was found that during this time he was exposed to stray radiation from 16 exposures and had travelled about 20 feet receiving a dose of 18 milliroentgens.

It is not without interest that this unlooked for irradiation of those in the waiting line is also reported in "Radiological Hazards to Patients" Ministry of Health, Department of Health for Scotland, Interim Report of the Committee, 1959, page 7. [See p. 1027.]

A list of exposures among patients is given in Table III, p. 116 from which very significant differences in dosage distribution were noted between men and women.

This seems a highly practical article of interest to all those engaged in mass radiography. *S. Russ*

GANATRA, R. D., with the technical assistance of R. Y. SAWANT. **Hematological Findings in Persons working in the X-Ray Department.** *Indian J. Med. Sci.* 1959, May, v. 13, No. 5, 393–400, 1 fig. on pl. [20 refs.]

This account of an investigation into the blood of people working in X-ray departments is of interest particularly because of the occurrence of lymphocytosis in spite of ordinarily safe working conditions.

The results were obtained from 8 hospitals in the Bombay district and the findings refer in the main to those people who worked in the X-ray diagnostic department.

The maximum permissible dose per year was 5γ and no one received as much as this. The mean lymphocyte count was higher in 34, out of a total of 73 people examined, to the extent of a lymphocytosis, and of these 34, blood smears of 15 of them showed abnormal bilobed or binucleated lymphocytes.

The author was unable to trace any relationship between this behaviour of the lymphocytes and the dose of X-radiation. He favours the view that the nature of the work, equipment and layout in the X-ray departments concerned, which were not in any way condemned, was nevertheless the important factor in establishing this condition of lymphocytosis in such a considerable proportion of the working staff.

S. Russ

SASLAW, S. & CARLISLE, H. N. **Effect of Total Body X-Irradiation on the Antibody Response of Monkeys.** *J. Lab. & Clin. Med.* 1959, June. v. 53, No. 6, 896–900, 1 fig.

Total body X-irradiation occurs normally in neither modern diagnostic nor therapeutic work; but the sustained interest in the subject arises from the conditions after an atom bomb explosion. Medical interest naturally centres upon those people who, situated at some distance from the centre of explosion, have suffered total body irradiation not enough to kill them, yet severe enough to make them critically ill. The possible and probable causes of death have often been reviewed in these columns largely from American literature.

The present study was carried out on young adult monkeys (*Macaca mulatta*). Various groupings of these animals were made and they were subjected to total body X-irradiation before or after typhoid immunization tests. X-rays at 250 KV were used filtered by 0·5 mm. Cu and 1 mm. aluminium, the dose given being 450γ. The protocols give full details of the standard tests carried out. The results were fairly clean-cut; the irradiation resulted in a temporary suppression of the antibody response of these monkeys when it took place 24 hours before the beginning of immunization, but no such effect was found when X-rays were given after the immunization. *S. Russ*

DAVIS, H. E. & PARKS, R. E. **Radiation Hazards resulting from Clinical Use of Radioactive Isotopes.** *Indust. Med. & Surgery.* Miami. 1959, May, v. 28, No. 5, 214–16.

There are no specific instructions to be found, in this account of the use of radioisotopes, on the avoidance of hazards to those using them in medicine. The chief of those in use are iodine and phosphorus, chromium, iron and cobalt, for diagnosis or treatment or both.

The chief hazards are by contamination in the laboratory where the preparations are made of and by ingestion of material which may become air-borne. There is also danger arising from the handling of radioactive excreta and this must always be supervised.

The hazard to the patient occurs when for instance significant quantities of an isotope are injected into the body to deal with a malignant growth; there may be radiation sickness and marrow depression. The treatment may yet be worth while if the malignancy is overcome.

In any radioisotope laboratory, non-absorbable aprons should be worn and shower facilities available in case of contamination. *S. Russ*

HYATT, E. C. **Health Hazards associated with Rolling Normal and Enriched Uranium—Evaluation and Control.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 82–91, 4 figs. [12 refs.]

This article describes the basic control measures required for safe operation in the rolling and other fashioning of Uranium.

Added to the already known toxic properties of Uranium there is radioactivity, alpha and beta in practice, the gamma radiation being very weak.

The health hazards are (1) inhalation of the oxide (2) external radiation (β) and (3) surface contamination. 3 is discussed in the article immediately following [below].

Uranium oxide is formed during the heating of the billets and sheets of the metal. The control measures are of the same general character as for other metals such as cadmium, selenium and tellurium. The enriched uranium carries more risk only because of its higher radioactivity. The chief precaution throughout is ventilation although much can be done by preventing the dust formation. As the author states "The days are gone when it was thought that poisonous dust could be blown out the window or over the roof and forgotten." The control measures for enriched uranium are

elaborate and costly. The working areas require cleanliness comparable with that of a modern kitchen. The work-room atmosphere and surfaces must be routinely monitored for alpha contamination. With the strictest controls in operation there is still some contamination, so penetrating is the fine oxide dust (particles of approximately 1 micron diameter). Surveys have been made over a period of five years and this gives weight to the importance of the work described. *S. Russ*

BLACKWELL, C. D. **Surface Contamination Control with Uranium Rolling Operations.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 92–8, 3 figs.

This article can usefully be read in conjunction with that immediately preceding it, as the work was all done at the same locations.

The author deals with contamination of equipment and its avoidance during the rolling of uranium into sheets. Samples were obtained by rubbing the areas with porous cloth or paper which is then tested for alpha-ray activity. If surfaces are covered with oil the alpha-ray tests are unreliable and recourse is had to beta-ray counts.

Constant vigilance throughout the whole series of operations is the key to safety and the detailed steps described here should be of the greatest value to those wanting to safeguard their employees. The author states that "with the exercise of proper contamination and fire control, the hazard encountered by personnel was nil". *S. Russ*

JOHNSON, W., KINDSVATTER, V. H. & SHAW, C. C. **Radiation Hazards abroad a Guided Missile Cruiser.** *U.S. Armed Forces Med. J.* 1959, May, v. 10, No. 5, 513–23, 2 figs.

The U. S. S. Galveston is the third ship in the U.S. Navy armed with guided missiles and the first such light cruiser equipped with the TALOS weapons system which directs the missiles to the target by high-powered radar beams. There are 2 radar systems, one to scan the sky and locate the target, the other to "lock" on target and track its evasive flight while the ship's guided missiles are prepared, launched and directed to intercept and destroy enemy planes.

Experimentally it has been shown that animals exposed to this microwave radiation can be damaged by cataract formation, corneal opacity and testicular degeneration. These are likely though not yet proved to occur in man if he is unduly exposed. The level of 10 milliwatts per sq.cm. of body surface has been arbitrarily established as a maximum safe level. An instrument known as a microline radiometer has been used to measure the strength of the radar emission at various position in the ship. Certain parts of the ship were found where the radiation was above that permitted and warning given to the personnel. While such measurements were being carried out, the operators wore copper meshed spectacles to protect the eyes from over-absorption; it was found that neon lamps will light up if held in these radar beams though the intensity is well within the safety range. This is made use of when testing by the operator putting these neon lamps inside their caps and when suspicious of undue radiation they take their caps off and judge by the light when to evacuate the position. A further potential danger on board arose from the X-rays given off by the Klystron tubes within the antenna domes of the radar gear. Here again regions in the vicinity gave much higher X-radiation values than would pass scrutiny; additional screening at the source met the situation. *S. Russ*

WHITSON, T. C. & KWASNOSKI, T. **The Determination of Alpha Activity associated with Sub-Microgram Quantities of Enriched Uranium in Urine.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 169–74, 3 figs.

"In summary, a procedure has been developed for routine determination of alpha activity resulting from the presence of sub-microgram quantities of enriched uranium in urine. Wet oxidation of the organic content, removal of the calcium, and two hours of electrodeposition have been found necessary prior to the alpha counting. The method provides over 80% recovery of the alpha activity with a precision of about ± 0.8 counts/minute."

NORWOOD, W. D. **The Determination of Injury from the internally deposited Radioisotope Plutonium.** *J. Occupational Med.* Chicago. 1959, May, v. 1, No. 5, 269–76. [35 refs.]

With increasing knowledge there has been a continued decrease in the maximum permissible amount of radium in the body as follows: In 1926 it was 10 microcuries, in 1936 1·0 microcurie, 1941 and to date 0·1 microcurie.

Although during 13 years of operation of plutonium (^{239}Pu) production hundreds of people have been so employed, no casualties due to this element have occurred; in fact the death rate is lower than that for the nation. This is accounted for by the general supervision of health that goes on. Nevertheless the author seeks to establish similar safety criteria for those working with ^{239}Pu as for ^{226}Ra. The chief difficulties are that weight for weight the radiation is not the same in these 2 cases and the measurements of body content are more difficult in the case of ^{239}Pu. The maximum permissible content is adjudged to be lower in this case. As the author states, it would have to be increased 100-fold to approximate the range at which statistically significant life-shortening has occurred in laboratory animals—reference here is to the work of R. H. MOLE—*Report of the United Nations Scientific Committee on the Effects of Atomic Radiation,* New York, 1958, p. 153, [this *Bulletin*, 1958, v. 33, 1155]. *S. Russ*

ARCH. MALAD. PROFESSIONNELLES. Paris. 1959, May–June, v. 20, No. 3, 258–71. Corps radio-actifs et pathologie professionnelle. Valeur des méthodes de surveillance des ouvriers. **[Radio-active Substances and Occupational Disease; Value of Measures for Supervising Workmen]** I. État

actual de la question [FOURNIER, E.], 258–62. II. Commentaires [FRANCHETEAU, G. & FOURNIER, E.], 262–3, 2 figs. III. Commentaires [TOULET, J.], 263–4. IV. Commentaires à propos de la décontamination [TOULET, J.], 265–7. V. Test biologique et prévention des accidents d'irradiation, 267–8. VI. A propos des examens biologiques systématiques [TOULET, J.], 268–9. VII. A propos des examens radiologiques [TOULET, J.], 269–70. Conclusions, 270–71.

The opening paper of this symposium by Fournier, as its title suggests, is a statement of present day methods of ensuring safety in radiation work and of the permissible levels of irradiation. A commentary by Francheteau and Fournier lays stress on the dangers of contamination following upon the use of radioisotopes. The skin is best cleansed by soap and water but abrasive powders should be avoided at all costs for they may do more harm than good. Further commentary by Toulet goes into the dangers of inhalation or absorption of various radioisotopes; he groups these under 3 headings: very toxic, moderately toxic and slightly toxic. Further commentary on the subject of contamination by Toulet gives minute instruction as to how external contamination should be dealt with, with special reference to a preparation, Montjoxydase, which is well tolerated by the skin. Regarding internal contamination, action must be prompt with a washout of the stomach, rhino-pharyngeal cleansing and intravenous perfusion. The same author discusses the practical value in detecting early radiation damage, of systematic blood counts and urinary examinations and in a following chapter comments on the dangers of radiological exposures. He challenges the finding of MACHT and LAWRENCE (U.S.A.) that the frequency of congenital malformations is higher among medical radiologists than among other medical people and quotes in his support the M.R.C. Report of 1956 [this *Bulletin*, 1956, v. 31, 1054]. *S. Russ*

TOULET, J.: TABERNAT, J. Contribution à l'étude des procédés de décontamination externe. Expérimentation d'un nouveau produit dans les cas de contamination radioactive des téguments. [**Decontamination of the Skin after Exposure to Radiation**] I. Principes généraux de décontamination externe. Éléments d'organisation pratique dans le cadre d'un centre d'études nucléaires [TOULET]. *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 272–6. II. Lotion "M.O. 8.385": Composition. Expérimentation dermatologique. Action décontaminante *in vitro* [TOULET & TABERNAT]. *Ibid.*, 276–8. III. Résultats cliniques [TOULET]. *Ibid.*, 278–82.

In the second seance of this symposium Toulet again discusses in great detail the general organization of safety in a nuclear centre.

After this exposition Toulet and Tabernat describe the properties and value of a new contamination eliminator Lotion "M.O. 8·385", containing no less than 20 ingredients and the final article, again by Toulet, gives the results obtained with this preparation in clinical work. *S. Russ*

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

JEBB, W. H. H. **A Comparison of Media for the Detection of Coliform Organisms in Water.** *J. Hygiene.* 1959, June, v. 57, No. 2, 184–92. [10 refs.]

The media chosen for this work were lactose broth, lauryl sulphate broth, Teepol broth, glucose glutamic acid medium and MacConkey broth, which has been the medium of choice in Britain for the isolation of coliform organisms for more than 50 years.

In all, 1,691 samples of water, chlorinated and unchlorinated, were examined over a period of 18 months at the Public Health Laboratory, Oxford.

The relative merits of the media are only comparable in waters which did not give the same results in all 5 test media and this occurred in 648 samples.

The total yield of coliform and *Escherichia coli* organisms was very much the same for all 5 media, but the majority of the *E. coli* isolated from MacConkey broth were obtained after only 18 hours' incubation. As experienced by previous workers, the yield of *E. coli* from glucose glutamic acid medium was the highest, but they were much slower in appearing.

There were large differences in the numbers of false presumptive positive results; the smallest numbers were obtained from MacConkey broth and 6 times as many were obtained from lactose broth.

The merits of a completely synthetic solution on the lines of glucose glutamic acid medium are discussed in the paper and it is recommended that such preparations are worthy of further investigation.

E. Windle Taylor

BUTTIAUX, R. Le controle bactériologique des eaux minérales. [**Bacteriological Control of Mineral Waters**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Mar., v. 7, No. 2, 131–47.

In this paper the author submits the results of his own research work at considerable length because of

the lack of published work on the control of the purity of bottled mineral waters. In France the mineral waters industry is of very great and characteristic importance.

The subject matter is set out in detail with description and discussion of bacteriological techniques and the standards of bacteriological purity which should be required. The paper is in 5 sections with many subsections. These cover: (I) the bacteriological control of the mineral water at the source, (II) the bacteriological control of the mineral water before, during and after bottling, (III) the standards of purity that are to be required at the source and in the bottling factory, (IV) the frequency with which bacteriological tests should be carried out and (V) the disposition and duties of laboratories which are charged with the task of carrying out bacteriological control. *M. E. Delafield*

See also p. 1039, GEVAUDAN, TAMALET & GAY, [**Comparative Survival of *Escherichia coli* and *Salmonella typhi* in Sea Water of the Mediterranean**].

FRASER, D. A. & FAIRHALL, L. T. **Lead Dissolution from Red-Lead Paints in Water.** *J. Amer. Water Works Ass.* 1959, May, v. 51, No. 5, 561–9, 9 figs. [10 refs.] [This paper appears also in *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 501.]

"Concern increases over the amount of lead taken into the body daily as it becomes more and more apparent from analyses of foods, air, and water that each source contributes a daily burden of lead to the body." It has been determined that the lead intake from sources other than water "dangerously approaches" the "maximum noncumulative daily body burden" of 0·5 mgm. of lead.

The purpose of the investigation described in this paper was to study the solubility of lead by water in contact with surfaces painted with red lead. 3 types of red-lead paint were investigated, *i.e.* (1) linseed-oil base, (2) phenolic base and (3) vinyl base. Measured areas of cleaned glass plates were painted, dried and immersed in water for varying periods after which the lead content of the water was determined by the chromate method and in some experiments by the dithizone method. Figures and description set out the results of the experiments on solution of lead from the 3 types of paints, the effect of drying time of oil-base paint, which dries slowly, on lead solution and the effect of successive leaching of oil-base paint on the amount of lead dissolved. Other experiments included study of the effect of residual chlorine, sodium hexametaphosphate, sodium hydroxide and hydrogen ion concentration on the solubility of lead in water.

The oil-base paint was found to yield at least 10 times more lead to the immersion water than either of the other 2 paints. The actual amounts of lead found were, in mgm. per litre of distilled water per 200 sq. cm. of painted surface, 7·4 for oil-base paint dried for 14 days, 0·3 for phenolic base paint and 0·2 for vinyl base paint. Residual chlorine increased lead solubility, sodium hydroxide lowered it and the effect of sodium hexametaphosphate varied with the concentration.

There is a full discussion. *M. E. Delafield*

ELKINS, H. B. **Lead Content of Water from Tanks painted with Red Lead.** *J. Amer. Water Works. Ass.* 1959, May, v. 51, No. 5, 570–74.

"During World War II, the question of the suitability of red-lead paints in tanks used for potable water was raised." As a result of the findings of "laboratory studies undertaken by the USPHS" that "some lead was dissolved from panels coated with red-lead paints" it was suggested that the use of such paints in tanks and standpipes for potable water should be prohibited.

The study described in this paper was undertaken at the request of the Lead Industries Association. It was begun in 1950 and has involved the lead analysis of 70 samples of water from 11 different standpipes coated with 3 different types of paint. Details are given of these paints. Tables and description give the results of the experiments. In only 3 of the samples of water was the permissible limit of 0·1 mgm. of lead per litre exceeded and these 3 samples were from "tanks in standby" service. The author in referring to the findings reported in the previous paper [see above] that lead dissolves freely from lead paints such as those used in these standpipes and which are apparently not reconcilable with his own results states "The obvious explanation is that the water does not stay in the tank long enough to pick up appreciable amounts of lead".

The conclusion is: "All the evidence available indicates that only under extremely exceptional conditions, if at all, could the use of lead paint in standpipes for potable water be considered inadvisable from the standpoint of the public health". *M. E. Delafield*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

GRUNE, W. N., BARTHOLOMEW, D. D. & HUDSON, C. I., Jr. **Effects of Radioactive Materials on Anaerobic Digestion. I. Radiophosphorus.** *Sewage & Indust. Wastes.* Wash. 1958, Sept., v. 30, No. 9, 1123–50, 9 figs. [52 refs.] **II. Radioiodine.** *Ibid.*, Nov., v. 30, No. 11, 1399–410, 9 figs.

I. The first part of the paper reviews comprehensively the present state of knowledge regarding the removal of radioactive isotopes by conventional sewage treatment methods. This is followed by a description of the authors' experiments on the effects of ^{32}P on anaerobic digestion, particularly the sterilizing effects of high concentrations of radioactive material. Total gas production was measured and the gases were continuously analysed by chromatographic techniques. Other continuous recordings were of *p*H, temperature, conductivity and oxidation-reduction potential, the last two being used to record the breakdown of solids and the reactivity of the substrate respectively. It was found that the ultimate gas production was reduced in the presence of 50 mc./litre of ^{32}P but it is thought that

this toxicity was a chemical rather than a radiobiological effect.

II. Using the same techniques as in Part I, the authors investigated the effect of ^{131}I on anaerobic digestion. They concluded that in concentrations up to 100 mc./litre ^{131}I had no significant effect. *A. James*

SPARGO, P. E. **Synthetic Detergents: Results of their Degradation on Johannesburg Sewage Works and Streams.** *Pub. Health.* Johannesburg. 1959, Apr., v. 25, No. 1, 11–25, 3 graphs. [14 refs.]

The paper opens with a review of the nature of synthetic detergents and of their reported effects on sewage treatment.

The concentration of anionic synthetic detergent in the raw sewage entering the Cydna treatment works of the City of Johannesburg varies between 1·5 and 30 p.p.m., averaging 4·6 p.p.m., which is about one-third of the average concentration in Britain. At 2 of the treatment works measurements showed that only about 5% of the detergent was removed in the primary settling tanks.

At the Cydna works 10–80% (average 50%) of the anionic agents was removed in biological filtration. At the same works the activated-sludge plant (presumably diffused-air system), which was producing a highly nitrified effluent, removed all the detergent; there was no foaming. One of the units at the Bruma works showed increasing foaming as nitrification decreased; foam appears at a relatively late stage of the aeration but not usually in the re-aeration channel. [The author can offer no explanation of this. The phenomena he reports are probably explained by the anti-foaming properties of soap, which is soon broken down, and by the higher solids concentration in the re-aeration channel, which results in greater adsorption of the detergent.]

Persistent foam occurs at a valve, through which the supernatant liquor from sludge digestion flows to a small pond.

Sand filtration of the effluent from humus tanks reduced the residual detergent concentration by up to one-sixth, the reduction increasing with time after the last cleaning of the filter.

Appreciable concentrations of synthetic detergent have been measured in streams receiving effluent from the Johannesburg sewage-treatment works and these had dropped by less than one-half after flowing 16 miles, at which point there was still appreciable foaming. Foaming occurs to a greater or less degree on all the City's works or after discharge from them.

Peter C. G. Isaac

LAPUCCI, P. Di un nuovo sistema per il trattamento dei liquami dei salumifici e dei macelli. [**A New System of Treating Meat-Packing and Slaughter-House Wastes**] *Riv. Italiana d'Igiene.* 1958, Nov.–Dec., v. 18, Nos. 11/12, 471–8, 1 fig. English summary (3 lines).

The author points out that trade wastes from meat manufacturing plants require both complex and expensive treatment largely because of the fat in colloidal suspension and the very high biochemical oxygen demand, and he then discusses the position as regards a plant dealing each week with a number of pigs and cattle where slaughtering was done on 2 days of the week only.

In view of the difficulty of dealing with the fat especially, chemical methods were tried. These included the use of aluminium sulphate, ferric chloride, an adsorbent—bentonite—and protein coagulants such as tannic acid, $CuSO_4$, and trichlor-acetic acid. Of these $CuSO_4$ gave by far the best results with a dose of 0·15 gm./litre, with a good floc which sedimented rapidly. Further tests, with 0·3 gm./l., and 0·5 gm./l., and 0·3 gm. $CuSO_4$ + 1gm.NaCl/litre were made but according to the table (2) the results after 12 hours were no better than with 0·15 gm./litre. The clarified liquid obtained was stable and could be run into almost any watercourse while the sediment dried easily and did not putrefy.

The author states finally that his opinion as exemplified by the above tests is supported by the good results of a plant operated on this method in Pistoia province and promises a special report on it.

[No details of the amounts of waste dealt with per day are given, so the promised report will be of considerable interest.] *W. K Dunscombe*

KLIMKINA, N. V. [**Hygienic Standards for Harmful Waste Products of the Synthetic Isoprene Rubber Industry contained in Water Basins.**] *Gigiena i Sanitariya.* Moscow. 1959, v. 24, No. 6, 8–16, 4 charts. [In Russian.]

The English summary appended to the paper is as follows:—

"With the synthesis by the method of M. I. Farberov isoprene and dimethyldioxane go into effluents. The presence of isoprene and dimethyldioxane in water gives it a foreign smell: the threshold value of smell for isoprene is 0.005 mg/l and that for dimethyldioxane 2.5 mg/l. Both of these products at concentrations below 30.0 mg/l have no effect on the biological processes of oxygen consumption by the organic substances in water. The sanitary toxicologic tests consisted in oral administration of each product for long periods of time.

"On the basis of the results obtained the author recommends the following maximum permissible concentration: for isoprene—0.005 mg/l, by its organoleptic properties, and for dimethyldioxane—0.005 mg/l by its toxic effect."

RODENT INFESTATION

BENTLEY, E. W. & LARTHE, Yvonne. **The Comparative Rodenticidal Efficiency of Five Anti-Coagulants.** *J. Hygiene.* 1959, June, v. 57, No. 2, 135–49. [20 refs.]

"1. Results are presented of palatability tests and chronic toxicity tests with five anti-coagulant rodenticides at a variety of concentrations against wild *Rattus norvegicus*, *R. rattus* and *Mus musculus*. These results

are compared with similar data for warfarin. Estimates are also given of the acute oral toxicity of two of the five, fumarin and diphacinone, to white rats.

" 2. The toxicity of the compounds *vis-à-vis* warfarin is examined from the standpoint of the risks to domestic animals involved in their use as rodenticides.

" 3. Coumachlor, 2-isovaleryl-1,3-indandione and 2-naphthyl-1,3-indandione are considered to be less effective than warfarin against *R. norvegicus*. Their effectiveness against *R. rattus* remains to be demonstrated.

" 4. Fumarin appears to be about as good as warfarin against *R. norvegicus* and *R. rattus* at similar concentrations. It appears to be slightly less effective against *M. musculus*.

" 5. Diphacinone at 0·0025% is regarded as a good alternative to 0·005% warfarin against *R. norvegicus*. At 0·0125% it is probably more effective against *R. rattus* than is 0·025% warfarin. The two poisons are about equally effective at this strength against *M. musculus*, but diphacinone is probably slightly more dangerous for domestic animals.

" 6. The results of a small number of field trials with fumarin and diphacinone are briefly summarized."

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

KOVACS, N. **Salmonellae in Desiccated Coconut, Egg Pulp, Fertilizer, Meat-Meal and Mesenteric Glands: Preliminary Report.** *Med. J. Australia.* 1959, Apr. 25, v. 1, No. 17, 557–9. [18 refs.]

This article from the Public Health Laboratory, Perth, Western Australia, reports the salmonella isolations from the various articles named in the title. In recent years there have been several reports on the high salmonella contamination of all these articles, with the exception of desiccated coconut. The actual salmonella sero-types vary considerably in the different reports but they agree in principle in establishing the fact that salmonella-contamination of these articles is a very frequent finding. Until the outbreak in 1953 of typhoid fever in Eastern Australia desiccated coconut had not, as far as is known, been considered as a health hazard. In this outbreak it will be recalled [see WILSON & MACKENZIE, this *Bulletin*, 1956, v. 31, 659] that Papuan desiccated coconut was incriminated epidemiologically, but that out of the many hundred samples examined by the different bacteriologists engaged on the enquiry only one specimen was found to contain *Salmonella typhi*. Nevertheless other salmonellae were isolated from coconut coming from the same area.

The present report deals with desiccated coconut imported from Ceylon from which *Salm. paratyphi B* was isolated as the sole salmonella sero-type on several occasions, but a variety of usual and unusual sero-types were present in other specimens. Because desiccated coconut is so frequently used in food-dishes where heat-treatment is not employed it is important that the potential dangers of this article of diet should be recognized. The present method of manufacture offers many opportunities for the contaminations found and unless this can be effectively modified it would appear that some form of sterilization of the product before issue for general use is essential; the author indicates that ethylene oxide was satisfactory for this purpose.

H. J. Bensted

FOOD POISONING

CALISTI, G. & DURANTI, G. Su di un grave episodio di tossinfezione alimentare da *Salmonella*. [**A Serious Food-Poisoning Incident due to Salmonella**] *Nuovi Ann. d'Igiene e Microbiol.* 1959, Mar.–Apr., v. 10, No. 2, 138–46.

This report gives more details on the food-poisoning incident at Osimo already reviewed [see this *Bulletin*, 1959, v. 34, 555] chiefly from the bacteriological angle.

The original epidemiological investigations having shown that the infecting salmonella was widely distributed in the food and had been recovered from the faeces of nearly all those attacked but not from the blood (15 specimens); the organism, which fermented rhamnose and was negative to all the sera available at the local laboratory, was sent to the laboratory at Pisa which is that for the study of pathogenic enterobacteria for central Italy. There it was identified as *Salm. typhi-murium* in phase 2 not belonging to " duck " type from the fact that it fermented rhamnose. The authors state that no strains of this type have hitherto been isolated from birds in Europe.

The method of infection seemed clearly to have been through the water in which the foodstuffs had been washed; how this became infected was not obvious, especially as 15 days previously another feast had been held, this time for threshing, which many, who were also at the second feast, attended and to which some from outside the province (Ancona) had come.

The organism was isolated from the faeces of pigs and ducks on the farm-colony, and from the spleen and liver of a goose, and the liver and kidneys of 2 ducks also living there. However, the authors suggest that the water may have been infected by some sylvatic

animal falling into it, or by a human carrier on account of the bad hygiene and the structural condition of the wells, as bacteriological examination of water samples showed the washing (and animal drinking) water to be heavily contaminated, and even the drinking water showed 15 coliforms/litre. *W. K. Dunscombe*

MASI, A. T., TIMOTHEE, R. A., ARMIJO, R., ALONSO, D. & MAINARDI, L. E. Dos brotes de envenenamiento por consumo de bacalao salado en Puerto Rico. [**Two Poisoning Outbreaks in Puerto Rico from Salt Preserved Codfish**] *Bol. Oficina Sanitaria Panamericana.* 1959, May, v. 46, No. 5, 465–71. [21 refs.]

The English summary appended to the paper is as follows:—

"The experience of two mass outbreaks and laboratory studies have been described to demonstrate the hazard of *Staphylococcus* intoxication which may result from salt preserved cod fish following extended exposure to water. Mention was made of the high salt tolerance of enterotoxigenic *Staphylococci* and of the commercial techniques of salting cod in order to support the view that the organism is not destroyed by the salt which is used in partially preserving this food. In fact the addition of suitable concentrations of salt may serve to kill spoilage bacteria which might compete for growth with the *Staphylococcus*. The value of using a 10% sodium chloride-nutrient medium in analysing specimens obtained from suspicious *Staphylococcus* intoxications was evident.

"The primary importance of a careful epidemiologic investigation with accurate food histories was illustrated. Experimental enterotoxin production studies will be necessary to clarify the role of the organisms isolated from both outbreaks."

POWER, J. G. P. & LISTER, H. **An Outbreak of *Clostridium welchii* Toxin Food Poisoning.** *J. Roy. Army Med. Corps.* 1959, Apr., v. 105, No. 2, 71–5.

In November 1956 a sudden outbreak of mild diarrhoea occurred in 2 of the 3 companies in a military camp. Its onset was in the early hours but none of the men were severely affected and all recovered quickly. At normal sick parade 66 men out of 500 at risk attended but only a few required treatment. There was evidence that about 50 more men with minimal symptoms did not report sick. Investigation indicated that a stew which was the main course at the tea meal on the previous day was the source of the infection. This stew had been prepared from fresh beef, peas, onions and a tomato purée made in the morning from tinned tomato soup heated up with bacon rind and bacon bones. From a sample of the stew, from rectal swabs or faeces of 14 out of the 26 patients who were investigated and also from the 6 cooks in the cookhouse, a heat-sensitive haemolytic *Cl. welchii*, type A, was isolated by the Public Health Laboratory Service. It was thought that the cooks had become infected through eating stew.

The conclusions were that probably the tomato purée was the source of infection and that the cooking temperature was insufficient to prevent further bacterial multiplication. It is mentioned that rodents and dogs may have been reservoirs of infection in this outbreak. *M. E. Delafield*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

WALTER, W. G. & CHAFFEY, Dorothy. **Bacteriological and Cleaning Studies on the Mouthpieces of Musical Instruments.** *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 126–30, 1 fig. [12 refs.]

Quantitative cultures were made from the mouthpieces of trumpets, trombones, saxophones and other wind instruments either immediately after use or 1 or 2 days later, and large numbers of bacteria were recovered (they were not identified, and it is thus not known whether they included pathogens). The band of the Montana State College, to which the instruments belonged, were then instructed to clean mouthpieces by brushing them after use with a detergent-sanitizer solution: the effect of this was to reduce the numbers of bacteria recoverable very greatly. Several different proprietary solutions were used, and all are considered to have been effective, but preference is expressed for one containing iodine, because as long as it retains its brown colour it is known by the user to be still active. Apart from the advisability of this precaution when an instrument may be used by different players, it is mentioned that "uncleaned mouth pieces develop unpleasant odors and became difficult to blow". *L. P. Garrod*

KAUDEWITZ, F. **Linear Transfer of a Potentially Mutant State in Bacteria.** *Nature.* 1959, Mar. 28, v. 183, 871–3, 5 figs.

SOC. EXPER. BIOL. **The Biological Replication of Micromolecules.** Symposia of the Society for Experimental Biology, No. 12.

This book was reviewed on p. 967.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

SIEGENTHALER, W. Die Bedeutung der alten und neuen Chemotherapeutica in Klinik und Praxis. [**The Significance of Old and New Chemotherapeutic Agents in Clinic and Practice**] *Schweiz. med. Woch.* 1959, Mar. 14, v. 89, No. 11, 275–84, 5 figs. [72 refs.]

This is an ambitious review of almost the entire field of antibacterial chemotherapy. The earlier part is illustrated by a table giving the chronology of discoveries in the synthetic and antibiotic fields, and by diagrams showing the sensitivity of different microbic species to sulphonamides and antibiotics, the rate of acquisition of bacterial resistance to different drugs, and the relationships between them as exhibited by cross-resistance. [These diagrams are interesting and helpful but open to criticism in some details. Separate diagrams are given for broad and narrow spectrum antibiotics: penicillin is included in the former but denied any action against species of *Haemophilus, Proteus, Salmonella* and large viruses, which alone would seem to justify such inclusion. Neomycin, which has in fact a very broad spectrum, is included in the narrow group, and is not credited with any action on *Mycobacterium tuberculosis.* Resistance to ristocetin and vancomycin does not develop as denoted in Fig. 3. Cycloserine acts on many other bacteria besides tubercle bacilli. The cross-resistance shown between chloramphenicol and the tetracyclines is not usual.]

The author then proceeds to describe the development of different sulphonamides and forms of penicillin and the clinical uses of these and the other antibiotics, concluding with separate consideration of those used in tuberculosis, protozoal infections, mycoses and as anti-tumour agents. An interesting development mentioned, unfamiliar in Great Britain, is a new form of tetracycline: this is Reverin (Hoechst), "a pyrrolidinomethyl tetracycline", which is said to be excreted in the bile to a much smaller extent than other tetracyclines, and thus to be less likely to cause enterocolitis.

Finally, the pros and cons of combined antibiotic treatment are discussed. One general conclusion reached is that broad spectrum drugs should be used by the practitioner and narrow spectrum drugs in the clinic, presumably because facilities exist there for verifying their applicability. [This seems a rule to which there could be frequent exceptions.] *L. P. Garrod*

REIMELT, Elisabeth. Eine Bakteriensprühapparatur für Testzwecke in der Antibiotikaforschung. [**A Bacteria Spraying apparatus for Test Purposes in the Study of Antibiotics**] *Zent. f. Bakt.* II. Abt. 1959, v. 112, Nos. 6/10, 264–73, 8 figs.

This paper describes an apparatus with which plates of culture medium can be inoculated by spraying a bacterial suspension on them. It is enclosed, and there is consequently said to be no danger of contamination of the atmosphere. It achieves uniform distribution of colonies, the numbers of which can be controlled by varying the density of the suspension and the duration of spraying: photographs show plates bearing a few hundred or many thousands of colonies. Cultures are also illustrated containing holes in which antibiotic solutions are placed, and sprayed with mixtures of bacteria, some of which are resistant to certain antibiotics: the purpose of this appears to be to identify an unknown antibiotic. Another plate sprayed with a mixture of 2 organisms bears a few colonies of *Streptomyces* spp. forming 3 different known antibiotics, which produce inhibition zones of different sizes. [The usual way to inoculate a plate uniformly is by flooding it with a bacterial suspension and draining. The relative merits of this and the proceeding described here are not discussed.] *L. P. Garrod*

LINZ, R. & LECOCQ, E. A propos des germes survivant à l'action bactéricide de la pénicilline. [**On Bacteria Surviving the Action of Penicillin**] *C.R. Soc. Biol.* 1958, v. 152, No. 12, 1839–41.

In a culture exposed to penicillin there are often a few survivors, and one explanation proposed for this is that these organisms are in a resting phase (BIGGER'S "persisters" [this *Bulletin*, 1945, v. 20, 39]). If so there are likely to be more in an old culture: the authors have tested this hypothesis and found it to be true. Agar slope cultures of *Staphylococcus aureus* and *Escherichia coli* 1 and 16 days old were suspended in saline and with this, broth was inoculated containing 1 and 1,000 units per ml. of penicillin respectively for the 2 organisms. After 24 hours survivors were enumerated and found to be more numerous in the tubes inoculated from the old cultures.

L. P. Garrod

BERNSTEIN, S. H. & HOUSER, H. B. **Sensitivity Reactions to Intramuscular Injection of Benzathine Penicillin.** *New England J of Med.* 1959, Apr. 9, v. 260, No. 15, 747–51. [16 refs.]

This paper describes reactions in United States Air Force personnel to doses of 1,200,000 units of benzathine penicillin given "as part of a general streptococcus-prophylaxis program". There were 2 series; 306 men given 1 dose, of whom 100 not reacting to the first were given a second 40 days later, and 611 men

of whom 308 were given penicillin and 303 an equal volume of sterile saline: in this group also a second dose was given to non-reactors. The types of reaction observed were "serum-sickness" [it is not quite clear what is meant by this], urticaria, maculopapular rash, arthralgia, pruritus, feverishness and pain at the site of injection. With the exception of the first-named, these occurred in men given saline as well as in those given penicillin, in some cases with equal or even greater frequency. The authors consider that 2% had a reaction genuinely attributable to penicillin, and conclude, on the basis of findings by others [this *Bulletin*, 1955, v. 30, 736], that a smaller dose is preferable. They also found that reactions very rarely occurred to a second dose when the first had produced none.

L. P. Garrod

See also p. 991, PELNER, **Allergic Reaction to Poliomyelitis Vaccine probably due to Penicillin.**

LÜCK, H. & RICKERL, Elisabeth. Lebensmittel-Zusatzstoffe und mutagene Wirkung. V. Mitteilung: Untersuchungen über die Erzeugung einer Streptomycinresistenz bei *Escherichia coli* durch Benzoesäure und p-Oxybenzoesäureäthylester. [**Additives to Foodstuffs and Mutagenic Action. Report V. Studies of the Production of Streptomycin Resistance in *Escherichia coli* by Benzoic Acid and *p*-oxybenzoic ethyl ester**] *Zent f. Bakt.* II. Abt. 1959, v. 112, Nos. 6/10, 226–34, 7 figs.

This investigation was made with the object of deciding whether bacteria exposed to the action of food preservatives may undergo undesirable mutations, *e.g.* to antibiotic resistance or to greater virulence. Benzoic acid was added in a concentration of 0·01 M to dense suspensions of *Escherichia coli*, and at intervals up to 2 hours aliquots were removed, washed and cultivated quantitatively in nutrient agar with and without the addition of 25 μgm./ml. of streptomycin.

When the *p*H of the suspension was 7·0 no change took place in the small proportion of streptomycin-resistant cells, but when it was 3·5 the total count diminished and the proportion of streptomycin-resistant cells increased. *p*-oxybenzoic acid ethyl ester behaved somewhat differently, there being some apparent mutagenic effect even at *p*H 7·0. However, any idea that these effects were specific was then negatived by the finding that both heat (56°C.) and suspension in an acid medium (*p*H 2·7) had a similar result, and the authors apparently conclude that to kill a proportion of a bacterial population by any means may lead to a higher frequency of antibiotic resistance among the survivors. These preservatives are therefore exonerated.

L. P. Garrod

PAKUŁA, R., HULANICKA, E. & WALCZAK, W. **Sensitivity to Ultraviolet Irradiation of the Streptomycin-Resistance Activity in transforming DNA of Different Bacteria.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 6, 217–22, 3 figs. [10 refs.]

KURKCUOGLU, M. & MCELFRESH, A. E. **An Anticoagulant Property of Antibiotics from Streptomyces Species. Its Possible Relation to Ecchymoses at Injection Sites.** *New England J. of Med.* 1959, Apr. 30, v. 260, No. 18, 926–7.

Determinations of clotting time and prothrombin time and thromboplastin generation tests were performed with the addition of different amounts of streptomycin, neomycin and kanamycin. The last-named test was unaffected: of the other two, detailed results are given only for the prothrombin time, which was prolonged by the addition of about 2,000 μgm./ml. of each antibiotic and considerably more by higher concentrations. This may be the mechanism or production of ecchymoses at sites of injection of concentrated solutions.

L. P. Garrod

HIRSCH, H. A. & FINLAND, M. **Antibacterial Activity of Serum of Normal Subjects after Oral Doses of Demethylchlortetracycline, Chlortetracycline and Oxytetracycline.** *New England J. of Med.* 1959, May 28, v. 260, No. 22, 1099–104, 4 figs.

Single doses of 500 mgm. of demethylchlortetracycline, with and without citric acid included in the capsules, oxytetracycline with glucosamine hydrochloride included in the capsules, and chlortetracycline without any such addition were given in rotation at 1-week intervals to 8 normal young men. Blood samples were obtained after 1, 3, 6, 12, 24, 48 and 72 hours, and assayed by 4 methods, 3 being tube dilution methods with different organisms and the other being *Bacillus cereus* plate assay. The averaged results are presented in tables and graphs in a variety of ways, but they may be interpreted briefly as follows. Citric acid did not affect the absorption of demethylchlortetracycline: with and without this addition the concentrations attained in the blood 1 and 3 hours after the dose were about the same as those of oxytetracycline and higher than those of chlortetracycline. Thereafter the curves diverge: demethylchlortetracycline increases in concentration up to the sixth hour while that of the other 2 diminishes, and then falls slowly, a detectable level persisting for so long that the most delicate assay method used detected antibiotic in every serum sample at 48 hours. These statements refer to w/v values, but in terms of activity, demethylchlortetracycline having a higher degree of activity than either tetracycline or oxytetracycline, the difference becomes considerably greater. [These findings confirm and do not greatly amplify those reported by KUNIN and FINLAND in the same journal not many months ago, this *Bulletin*, 1959, v. 34, 369.]

L. P. Garrod

DOMZ, C. A., MCNAMARA, D. H. & HOLZAPFEL, H. F. **Tetracycline Provocation in Lupus Erythematosus.** *Ann. Intern. Med.* 1959, May, v. 50, No. 5, 1217–26, 1 fig. [48 refs.]

"Three patients are described in whom L. E. reactions occurred after administration of tetracycline. These reactions, and L. E. reactions to other drugs, may take three forms:

"1. *De novo* appearance of systemic L. E.

"2. Exacerbation of known L. E.

"3. Positive L. E. tests without clinical signs or symptoms of L. E. Circumvention of such reactions depends upon the physician's awareness of the sensitizing potential of the medications he employs, and vigilant conservatism in their use."

SMITH, I. M. & SODERSTROM, W. H. **Clinical Experience with a New Erythromycin Derivative, Erythromycin Propionate. Report of One Hundred Five Cases.** *J. Amer. Med. Ass.* 1959, May 9, v. 170, No. 2, 184–8. [12 refs.]

Erythromycin propionate, which is better absorbed and produces higher blood levels than erythromycin in the forms previously used, was given to 105 patients, usually in a dose of either 0·25 or 0·5 gm. 4 times a day, with good results in 98 of them. Most of these had staphylococcal infections, classified as pustular acne, boils, carbuncles, other pyodermas, ulcers, osteomyelitis and pharyngitis: there were also 14 patients with streptococcal pharyngitis: other infections of the air passages, caused by various bacteria, were bronchitis, pneumonia and sinusitis. 5 illustrative case histories are given. Gastro-intestinal side effects occurred in 8 patients (anorexia, nausea, vomiting or diarrhoea) and are described as "minor in degree", but elsewhere it it said that treatment was discontinued in 3 on account of them. *L. P. Garrod*

DEARING, W. H. & NEEDHAM, G. M. **Effects of Oral Use of Neomycin plus Bacitracin on Intestinal Flora of Man.** *Proc. Staff Meetings Mayo Clinic.* 1959, Mar. 4, v. 34, No. 5, 127–31.

Patients awaiting intestinal surgery were given a low residue diet, saline cathartics, and either 1 gm. neomycin and 5,000 units of bacitracin 4 times a day (29 patients), or 5,000–20,000 units bacitracin only 4 times a day (6 patients). Stools were cultivated 1, 2 or more days later by what appears to have been a roughly quantitative method [for a description of this and the results of giving neomycin alone the reader is referred to an earlier paper, this *Bulletin*, 1954, v. 29, 308]. Bacitracin alone had no apparent effect and its combination with neomycin had an effect indistinguishable from that of neomycin alone in the previous study. It is suggested that bacitracin may be useful from the 4th day after operation in preventing the invasion of the bowel by staphylococci, when the normal flora has been suppressed by previous treatment with neomycin or neomycin + tetracycline. *L. P. Garrod*

HERTING, R. L., LEES, B., ZIMMERMANN, A. J. & BERRYMAN, G. H. **Ristocetin—a Statistical Review of Three Hundred Thirty-Three Cases.** *J. Amer. Med. Ass.* 1959, May 9, v. 170, No. 2, 176–8.

The authors are on the staff of Abbott Laboratories, manufacturers of ristocetin, and what they have done is to take all clinical records of therapy with this antibiotic, whether published or communicated personally to them, and analysed them "by machine methods". There were 333 cases, including 126 of pneumonia, 46 of subacute bacterial endocarditis, and 38 of septicaemia, the rest being various septic conditions in 11 different categories. Causative bacteria were staphylococci in 211, streptococcus, pneumococcus and enterococcus in 12, 10 and 11, mixed in 16 and unknown in 73. Recovery rates are given for organisms only, not by clinical diagnosis: thus the only significant figure is for staphylococcal infections, among which 118 were cured, 44 improved and 49 showed no response. Side effects included neutropenia in 18 cases, drug fever in 12, skin rash in 14: the incidence of these was more than doubled by increasing the dose to over 2 gm. daily. Thrombophlebitis, consequent on necessarily intravenous administration, occurred in 20 cases. [This analysis is not very helpful, except in indicating the desirability of limited dosage—assuming this to be effective. A clearer indication of the value of ristocetin might have been given by stating the percentage of recoveries in the 84 patients with infection of the blood stream.] *L. P. Garrod*

THORNLEY, Margaret J.; YUDKIN, J.; SINAI, J. **The Origin of Bacterial Resistance to Proflavine. 1. Training and Reversion in** *Escherichia coli* [THORNLEY & YUDKIN] *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 355–64, 9 figs. **2. Spontaneous Mutation to Proflavine Resistance in** *Escherichia coli* [THORNLEY & YUDKIN] *Ibid.*, 365–72, 2 figs. **3. The Alleged Rapid Adaptation to Proflavine Resistance in** *Bacterium lactis aerogenes* (syn. *Aerobacter aerogenes, Klebsiella pneumoniae*) [SINAI & YUDKIN] *Ibid.*, 373–83, 5 figs. **4. Cycles of Resistance in** *Escherichia coli* **and their Bearing on Variations in Resistance in Cultures** [SINAI & YUDKIN] *Ibid.*, 384–99, 8 figs. **5. Transformation of Proflavine Resistance in** *Escherichia coli* [SINAI & YUDKIN] *Ibid.*, 400–413. [14 refs.]

These 5 papers describe an extensive study of the mode of acquisition of bacterial resistance to proflavine hemisulphate: this substance was chosen because it is that used by HINSHELWOOD and his colleagues in many experiments which are said to show that resistance results from specifically induced adaptation. The present authors worked chiefly with a strain of *Escherichia coli*, from which various other designated "strains" were obtained by sub-cultivation processes. The general conclusion reached is that although a minor degree of adaptation can occur, acquired resistance is mainly the result of mutation. The nature of the experiments and the main findings were as follows:—

1. Cultures were made in broth with and without proflavine and the distribution of resistance determined by dilution and plate counts and by streaking on gradient plates. The results differed from those of Hinshelwood *et al.* in that resistance developed to a considerably higher concentration of proflavine than that to which the organism had been exposed, and persisted in normal medium despite only short exposure.

2. After inconclusive experiments with the fluctuation test, resistant mutants having had no contact with proflavine were obtained by the method of indirect selection by replica plating. A 3rd-step mutant so obtained

was about 100 times more resistant than the parent culture. Mutants resistant to chloramphenicol were obtained in the same way, and cross-resistance between the 2 substances was observed.

3. The rapid adaptation to proflavine in "*Bacterium lactis aerogenes*" observed by BASKETT [this *Bulletin*, 1952, v. 27, 779] when successive additions of proflavine are made to a culture at short intervals is shown in several ways to have been due to acid formed from glucose in the medium. It did not occur in *E. coli* grown in broth.

4. Small amounts of proflavine were added to cultures at intervals varying from 30 to 315 minutes after inoculation. Addition after 125 minutes caused a large proportion of the organisms to acquire a moderate degree of resistance, a change which the authors regard as adaptive: it was unaccompanied by any increased resistance to other drugs. Similar variations in adaptability occurred cyclically in cultures in which division was synchronized by cooling.

5. Extracts of resistant organisms were prepared in various ways with the object of transforming sensitive cultures to resistance, a result which the authors consider to be proof that resistance has a genetic basis. A small proportion of these attempts were successful.

L. P. Garrod

ZAEVA, S. P., ALEKSEEVA, L. N., RATENBERG, N. S. & KOPTELOVA, M. N. **An Experimental Study of the New Chemotherapeutic Preparation Furazidine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 7, 1022–7. [Translated from Russian.]

Furazidine is said to be a new and original compound of the nitrofuran series, and was synthesized in the Institute of Forestry of the Academy of Sciences of the Latvian S.S.R. Chemically it is N-(5-nitro-2-furylallylidene)-1-aminohydantoin. It was found to inhibit the growth of 25 species of bacteria, both Gram-positive and Gram-negative, in concentrations of < 1 and sometimes $< 0{\cdot}1$ mgm.% *Proteus vulgaris* was a little more resistant, and against *Pseudomonas pyocyanea* the substance was inactive. Blood, serum or pus did not interfere with its activity.

Mice were inoculated intraperitoneally with *Shigella flexneri* or *sonnei*, *Salmonella typhi*, *Escherichia coli* or *Staphylococcus aureus* and given Furazidine by mouth: the LD50 of the culture in mice so treated was higher than in the controls. A few survival figures are also given (*e.g.* 22 out of 35 treated and 11 out of 35 controls in *Staph. aureus* infection).

Finally various studies of toxicity are described, the results of which were satisfactory. The authors conclude that "Clinical trial of furazidine in intestinal and wound infections is indicated". *L. P. Garrod*

ZAEVA, S. P., ALEKSEEVA, L. N., RATENBERG, S. N., KOPTELOVA, M. N., MEDNE, K. K. & SPURE, I. P. **Experimental Study of the Drug Furazolidone.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 7, 1027–32. [Translated from Russian.]

This paper is very similar to the foregoing [see above]. Furazolidone (N - (5 - nitro - 2 - furfurylidene)-3-amino-2-oxazolidone) is rather more active *in vitro* than Furazidine against *Salmonella* and *Shigella* spp., but less active against 3 species of *Clostridium* tested (no end-point given). Therapeutic tests in mice are very briefly described, the infections studied being almost the same but including *Salmonella typhi-murium*, against which Furazolidone was found to be more effective than chloramphenicol. [In this and the previous paper not enough is said about how these experiments were done or about details of the findings to permit assessment of their significance: such actual figures as are given do not indicate a very clear-cut result.]

Finally, various tests of toxicity are reported, showing that the lethal dose is very high, and that the prolonged administration of moderate doses has no ill-effects.

L. P. Garrod

CHENCHIKOVA, E. P. & SHAVYRINA, V. V. **The Sporocidal and Bactericidal Properties of 1 : 3-Dichloro - 5 : 5 - Dimethylhydantoin.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 1151–4. [Translated from Russian.]

This report from the Central Institute of Disinfection of the U.S.S.R. records the preparation of 1 : 3-dichloro-5 : 5-dimethylhydantoin following reports from abroad of its bactericidal activity. It is said to contain 70% of active chlorine (compared with about 26% in chloramine or chloride of lime) and is stable as a solid: its solubility in water is only 0·3% at 60°C. Its action was tested by immersing strips of cotton fabric on which bacterial suspensions had been "dried" in solutions of different strengths, removing a strip at intervals, treating it in thiosulphate solution and cultivating it in broth. (The strips were "dried with sterile filter paper, and the last traces of moisture were removed by incubation for 30 min.") The organisms used were *Staphylococcus aureus*, which was killed by a 0·006% solution in 10 minutes, and "pseudoanthrax" spores, killed by 0·12% in 35 minutes. This represents about 10 times the activity of chloramine. Solutions "activated" by added ammonium chloride were more rapidly sporicidal. *L. P. Garrod*

DEUT. GESELLSCHAFT F. HYG. U. MIKROBIOL. [KLIEWE, H., Chairman.] Richtlinien für die Prüfung chemischer Desinfektionsmittel. [**Correct Procedures for Testing Chemical Disinfectants**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 307–17.

This is a report of a committee of the German Society for Hygiene and Microbiology which was instructed to define satisfactory procedures for testing chemical disinfectants. It describes 15 methods designed for different purposes in some detail, but not enough to ensure strictly reproducible results: among variables not provided for are the composition of the culture media, inoculum size, strain of organism and others. Neutralizing agents are specified for the more important classes of disinfectant to prevent growth inhibition by carry-over.

The methods are divided into 2 classes, the first consisting of tests under purely laboratory conditions and the second embodying various aspects of practical use. Included in the former are a simple test of growth-inhibitory action, tests of bactericidal action by the suspension method (*i.e.* the addition of a suspension of the organism to a series of disinfectant dilutions and subsequent cultivation of the mixtures), instructions being given for preparing suitable suspensions of vegetative bacteria, bacterial spores and fungi, and similar tests by the "carrier" method, the carriers being garnets, glass beads or pieces of fabric. The uses provided for in tests in the second category are skin disinfection, the disinfection of fabrics (contamination by tubercle bacilli and by other pathogenic vegetative bacteria being separately considered) of floors and other surfaces, and of excreta. In some connexions it is suggested that a comparison should be made with the action of a standard substance (*e.g.* 0·1% hexylresorcinol in tests with fungi and 80% ethanol in tests of skin disinfection). The methods described are all such as have been conventional for many years.

L. P. Garrod

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

GEVAUDAN, P., TAMALET, J. & GAY, R. Étude de la survie comparée d'*Escherichia coli* et de *Salmonella typhi* dans l'eau de mer du littoral méditerranéen. [**Comparative Survival of *Escherichia coli* and *Salmonella typhi* in Sea Water of the Mediterranean Coast**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 128–37.

A careful comparison was made of the survival in sea-water of small inocula of a standard strain of *Escherichia coli* (E 36) and of 2 stock typhoid strains, one containing Vi antigen (Ty 2) and one without (Ty 0·901). The organisms were inoculated into 200 ml. of the following: natural sea-water taken far out at sea or from clean beaches with no demonstrable *E. coli* or phage in 50 ml. volumes; sea-water filtered through an L.3 candle, and sea-water so filtered and also autoclaved at 120°C. Double-distilled sterile water of *p*H 7·2 was used as control. In 2 comparative experiments with E 36, a viable inoculum of 5,000 organisms per ml. of sea-water was used in one, and of 250 per ml. in the other. In one experiment with Ty 0·901, a viable inoculum of 500 per ml. of sea-water was used; in 2 experiments with Ty 2, one done at 37°C. used an inoculum of 125 organisms per ml. and one done at 20°C. an initial inoculum of 700 per ml.

The results obtained were clear-cut. With the larger inoculum of E 36, the distilled water control flasks showed a steady death-rate, with a small number of viable organisms present for up to 14 days. In natural sea-water virtually all the organisms had perished after 48 hours. An intermediate duration of survival for up to 5 days was observed with filtered, autoclaved sea-water. With inocula of 250 per ml. of E 36, survival in distilled water was demonstrated for up to 5 days, and survival time in sea-water was correspondingly curtailed. Both typhoid strains showed a very similar viability to that of *E. coli* strain in experiments with comparable inocula.

B. Moore

KIESEWALTER, J. Untersuchungen über die Verwendbarkeit des O–1 Phagentestes zur *Salmonella*-Diagnose. [**Study of the Suitability of the O–1 Phage Test in the Identification of Salmonellae**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 2, 190–95.

The O–1 phage test, as used by CHERRY *et al.* [this *Bulletin*, 1955, v. 30, 355] for the screening of salmonella strains, was applied by the author to a number of standard strains of Enterobacteriaceae and to strains isolated from clinical material.

In all, a series of 1,388 *Salmonella*, Arizona, *Escherichia, Shigella, Proteus* and *Citrobacter* strains were investigated. 192 representative salmonella serotypes were included. Among the other organisms tested were 18 cultures from various groups of Enterobacteriaceae sharing common antigens with salmonellae.

The results are tabulated and discussed. Of 603 *Salmonella* strains, only 26 (4·31%), falling into 16 different serotypes, showed no lysis in the 0–1 test. None of 204 *Shigella* strains, of 76 Bethesda-Ballerup strains, or of any other groups except *Escherichia* and the Arizona group, showed any lysis. But 19 (4·14%) of 459 *E. coli* strains gave a positive result, as did 2 Arizona strains—both diphasic—in a series of 25 strains examined.

B. Moore

THOMASON, Berenice M., CHERRY, W. B. & EDWARDS, P. R. **Staining Bacterial Smears with Fluorescent Antibody. VI. Identification of Salmonellae in Fecal Specimens.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 478–86, 2 figs.

"The potential value of employing fluorescent antibody solutions for the direct identification of salmonellae in fecal smears has been investigated. Cross serological reactivity was a serious problem as shown by the results of studying pure cultures of various *Enterobacteriaceae.* This was confirmed by further studies of fecal specimens from typhoid carriers, from patients with gastroenteritis, and from normal persons. At the present time, no method has been found to resolve this difficulty although it is postulated that the problem may be less important in certain specialized areas of application. It appears that incomplete antibody may influence the interpretation of fluorescent antibody tests to a significant degree and that these tests constitute an effective tool for measuring the prevalence

of this antibody. The importance of analysing pre-immunization sera to prevent misleading interpretations of fluorescent antibody tests is stressed. Variations in types of staining reactions obtained are pointed out and their significance discussed. The value of fluorescent antibody as a tool for the study of cellular architecture is emphasized."

RISCHE, H. & SCHNEIDER, H. Die Unterteilung des Typhusbakterien-Lysotyps E_1. [**Subdivision of Typhoid Bacilli Lysotype E according to Brandis**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, May–June, v. 5, No. 3, 188–91.

The English summary appended to the paper is as follows:—

"Amongst 1966 patients (1211 cases of acute illness and 755 carriers of germs) it was possible to ascertain the subtypes E. a and E. b (table 2). Calculated by focal infections (table 3) the proportion of subtype E. a to subtype E. b is about 2 : 1. The practical constance of the subtypes could be proved on the strength of 10 epidemics and 99 smaller contact chains (table 4). Animal experimental investigation with rabbits and guinea pigs showed the same results."

SCHAECHTER, M., MAALOE, O. & KJELDGAARD, N. O. **Dependency on Medium and Temperature of Cell Size and Chemical Composition during Balanced Growth of** *Salmonella typhimurium. J. General Microbiol.* 1958, Dec., v. 19, No. 3, 592–606, 4 figs. [28 refs.]

KJELDGAARD, N. O., MAALOE, O. & SCHAECHTER, M. **The Transition between Different Physiological States during Balanced Growth of** *Salmonella typhimurium. J. General Microbiol.* 1958, Dec., v. 19, No. 3, 607–16, 4 figs.

KHOMIK, S. R. & GALAEV, I. V. **Biochemistry of Amino Acid Metabolism in** *Salmonella typhimurium* **(Breslau).** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 547–52. [Translated from Russian.]

DOTTI, F. & CASETTA, R. Patogenicità e fimbriatura in *Salmonella typhimurium.* [**Pathogenicity and Fimbriation in** *Salmonella typhimurium*] *Igiene Moderna.* 1959, Jan.–Feb., v. 52, Nos. 1/2, 21–8, 4 figs.

The English summary appended to the paper is as follows:—

"The authors question the possible relationship between fimbriature and pathogenicity in pathogenic microorganisms. They have observed a greater mortality in mice which have been inoculated with a fimbria-less *Salmonella typhimurium* compared with the mortality of mice which have been inoculated, *coeteris paribus,* with a fimbriated variant of the same *Salmonella.*"

GRABAR, J., with the technical collaboration of Marie T. VINAY. Action sur les tissus de la souris de certains vaccins, préparés avec des souches de *Salmonella* pathogènes et non pathogènes pour cet animal. [**Tissue reactions of Mice to certain Vaccines prepared from** *Salmonella* **Strains, Pathogenic and Non-Pathogenic for mice**] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 577–90, 5 figs. on pl. [16 refs.]

Heat-killed vaccines of smooth salmonellae injected into mice in doses varying from 10×10^6 to 40×10^6 appear to give rise to a non-specific toxic reaction in the liver; this was not observed with a vaccine made from a rough strain of the typhoid bacillus. Typhoid bacilli and some strains of paratyphoid A are non-pathogenic for mice, whereas *Salmonella paratyphi B, Salm. typhi-murium* and *Salm. enteritidis* are pathogenic for these animals. And there is a very significant difference in the tissue reactions following the injection of the 2 types of living vaccine; the pathogenic type provokes early glandular involvement which quickly develops into an acute inflammatory lesion whereas the living non-pathogenic type, although it may lead to some toxic tissue reaction, does not produce any glandular changes. Mice that have received killed vaccines of paratyphoid B or *Salm. typhi-murium* and are challenged 10 days later with a homologous culture show a reticular endothelial reaction which tends to regress. There is no evidence of acute glandular involvement owing to the developing immunity from the first vaccine. *H. J. Bensted*

LE MINOR, L., THOME, M., PERREAU, P. & CHARIE-MARSAINES, C. Un nouveau sérotype de *Salmonella: S. Farcha.* [**A New** *Salmonella* **Serotype:** *S. Farcha*] *Ann. Inst. Pasteur.* 1959, July, v. 97, No. 1, 107–8.

The English summary appended to the paper is as follows:—

"Description of a new *Salmonella* serotype, *S. farcha,* isolated from mesenteric nodes in goats at Fort-Lamy (Tchad)."

[The formula is 43 : *y* : 1,2.]

VANĚCEK, J., RASKOVA, H., JELÍNEK, J., RASKA, K. & MATĚJOVSKÁ, V. **The Changes of** *Shigella shigae* **Toxin Toxicity induced by Phenol.** *Brit. J. Exper. Path.* 1959, June, v. 40, No. 3, 203–8, 1 fig. [14 refs.]

This group of workers had previously shown (RASKOVA *et al., Časopis Lékařů Českých.*, 1952, v. 91, 1348) that the application of Shiga toxin or streptolysin O to the sciatic nerves of cats or rabbits resulted in identical conductivity changes leading to complete block. Analogous phenomena were seen when phenol was used in place of the other substances. Immunization of the animals with, for example, Shiga toxin afforded protection not only against the effect of the local application of Shiga toxin, but also against the effect of streptolysin O, and even phenol. Moreover, further experiments indicated that rabbits, pre-treated

with solutions of phenol, developed some degree of protection against the effects of Shiga toxin applied locally at a latter date.

In order to find out how this phenomenon was related to the general effect of toxin, as measured by LD50 changes, mice were subcutaneously injected twice weekly with 0·05 ml. of a 0·1% solution of phenol. After various series of doses, ranging from 3 to 15, the LD50 of the Shiga toxin was determined in these phenol-treated animals and also in control groups of mice from the same litters by injecting the standardized toxin intraperitoneally in a regular range of doses. When the number of injections of phenol, in the pre-treatment programme, reached 9 there was a significant development of resistance to the effect of the Shiga toxin. A side experiment testing the possible effect of arsenic trioxide instead of phenol was negative.

The experiments described in this paper are of very considerable interest, but the account does not offer a satisfactory explanation of the phenomenon.

H. J. Bensted

LURIA, S. E. & BURROUS, Jeanne W. **Hybridization between** *Escherichia coli* **and** *Shigella*. *J. Bacteriology*. 1957, Oct., v. 74, No. 4, 461–76. [38 refs.]

"A number of Shigella strains were tested for mating ability with *Escherichia coli*. All the strains tested were fertile with F+ or Hfr derivatives of *E. coli* strain K-12 and *E. coli* strain C. The Shigellas behave like F− strains in the fertility system of *E. coli* and, like *E. coli* F−, can be changed to the F+ state by mixed cultivation with an F+ culture. Matings result in formation of hybrids, which exhibit new combinations of characters typical of Shigellas with characters typical of *E. coli*. The frequency of recombination is lower than in similar crosses between strains of *E. coli*, although the frequency of mating, measured by zygotic induction of prophage λ, is comparable in both types of crosses. Also, some of the characters of the coli parent fail to be transmitted to the *E. coli* × Shigella hybrids. These results suggest an incomplete genetic homology between the two groups of organisms.

"Some hybrids between *E. coli* and type strains of *Shigella flexneri* possess somatic antigens closely related to those of *S. flexneri* type Y. This antigenic change is controlled by genetic factors closely linked to factors controlling lactose utilization. The results suggest a possible role of hybridization occurring in nature in the evolution of the *Enterobacteriaceae* and in the origin of aberrant and intermediate strains of enteric bacteria."

TAYLOR, Joan. *Escherichia coli* **as an Enteropathogen**. *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 357–63. [39 refs.]

This paper is essentially a review presenting the history of the type specific strains of *E. coli* and giving the salient points of the investigations which have led to the belief that these strains are enteropathogens. The organisms are traced from their first isolation in 1886 by ESCHERICH, through the early work of ADAM to the serological researches of BRAY, GILES and SANGSTER, SMITH, TAYLOR and KAUFFMANN; among the later investigations described are the "ligated loop" experiments initiated by DE and his co-workers [this *Bulletin*, 1957, v. 32, 279] and the work on diarrhoea in calves. The addition of a comprehensive bibliography combines to make this review a valuable reference work.

John S. Stevenson

ROGERS, K. B., DOWSE, J. E. & HALL, J. T. **Techniques used in the Routine Examination of Specimens for the Specific Serological Types of** *Escherichia coli*. *J. Clin. Path.* 1959, Mar., v. 12, No. 2 191–2.

This is mainly a description of the techniques used by the authors for the rapid indentification of *Escherichia coli* serotypes. By carrying out the slide agglutination screening before 10.30 a.m. a 4-hours' broth culture can be obtained from a positive colony: portions of this broth can be killed by boiling and with 1/1,000 mercuric iodide for O and K agglutination respectively, the centrifuge being employed to hasten the tests. This is claimed by the authors to produce rapid diagnostic confirmations which can be transmitted to the wards concerned. [The abstracter is doubtful if this speedy tube-testing is of direct practical value, considering the amount of work involved. While it is true to say that every *E. coli* serotype should be accurately diagnosed, it must be remembered that most paediatricians do not base their treatment on the result of a tube test, rapid or otherwise.] *John S. Stevenson*

WOLLMAN, E. L. & JACOB, F. Sur les processus de conjugaison et de recombinaison chez *Escherichia coli*. V.—Le mécanisme du transfert de matériel génétique. [**The Process of Conjugation and Recombination in** *E. coli*. **V. The Mechanism of Transfer of Genetic Material**] *Ann. Inst. Pasteur*. 1958, Dec., v. 95, No. 6, 641–66, 5 figs. [21 refs.]

The English summary appended to the paper is as follows:—

"1. Bacterial conjugation involves two main steps: the formation of the zygotes and the formation of genetic recombinants. The first one extends from the encounter of two bacteria of opposite mating type to the completion of a zygote by transfer of genetic material from donor to recipient. The second one, which takes place in the recipient which has become a zygote, extends until the formation of a clone of recombinant type.

"2. In the formation of the zygotes, one may distinguish three successive steps: the collisions between bacteria of opposite mating types which lead to the formation of effective contacts or specific pairing, which are followed by transfer of genetic material from the donor to the recipient bacterium.

"3. The effective contacts begin as soon as the bacteria of opposite mating types are mixed. They resist dilution when gently made. In the usual conditions of a cross, all possible conjugations take place in less than 25 minutes.

"4. Genetic transfer consists in the oriented and progressive penetration of the Hfr chromosome into the F− bacterium. It is always the same extremity or

origin, O, of the Hfr chromosome which penetrates first, followed in a predetermined order by the various genetic determinants of the Hfr bacterium. In the usual conditions of a cross, the penetration of the whole Hfr chromosome takes about two hours.

"5. During the slow progression of the Hfr chromosome, spontaneous ruptures occur, so that, for a genetic character, the farther its location from the proximal end O of the Hfr chromosome, the smaller the chance of its transfer. The probablity of rupture of the Hfr chromosome, and thus the probability of transfer of a distal character are strongly dependent on the experimental conditions (shaking, dilutions, time of plating).

"6. The interruption of conjugation, and hence of genetic transfer, may be achieved at will by stirring in a Waring blendor. This treatment is without effect on the survival of either parental types or zygotes. The time at which any given genetic determinant has been transferred from Hfr donor to F − recipient may thus be determined with precision and a genetic map of the Hfr chromosome be drawn in time units.

"7. The penetration of the Hfr chromosome occurs at a roughly constant speed along the first half of its length. The genetic map in time units appears therefore to afford a satisfactory representation of the physical distance between genetic determinants. It is thus made possible to relate genetic and physical measures.

"8. Transfer being partial in the great majority of the cases, the zygotes formed are incomplete zygotes or *merozygotes*. Bacterial conjugation may thus be brought together with the other known modes of genetic transfer in bacteria (transformation and transduction) and the name *meromixis* has been coined to designate those processes of partial transfer or incomplete fertilization whereby merozygotes are formed which are essentially constituted by the recipient cell and only part of the genetic material of the donor cell."

BARTLETT, G. W. & HINSHELWOOD, C. **Observations on the Drug Resistance of Bacterial Recombinants.** *Proc. Roy. Soc.* Ser. B. 1959, Apr. 21, v. 150, No. 940, 318–35. [17 refs.]

"Strains of *Escherichia coli* '*K*-12', sensitive or resistant to chloramphenicol, proflavine or brilliant green were crossed, and the drug resistance of the recombinant strains examined. For this purpose a quantitative scale of resistance was established, so that the spectrum of the distribution among the recombinants could be determined.

"In general, the recombinants showed a continuous spectrum of resistances in the complete range between the values for the two parent strains, with a greater probability of values towards the middle of the range. When both parents were resistant no recombinant showed resistance appreciably greater than the higher of the parental values.

Parent strains proved to be of two types (probably identifiable with the donors and receptors of other workers) such that the cross $A_{\text{resistant}} \times B_{\text{sensitive}}$ gave a nearly complete recovery of parental units of resistance, while the cross $A_{\text{sensitive}} \times B_{\text{resistant}}$ gave a much smaller recovery.

"The interpretation of these results is discussed in general terms."

KOCH, A. L. **Death of Bacteria in Growing Culture.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 623–9. [24 refs.]

"In growing cultures of *Escherichia coli* maintained under constant conditions, cell death followed by lysis is a rare phenomenon. If, however, the cells are chilled and centrifuged, approximately 5 per cent per hour of a variety of labelled cellular components are released into the growth medium in an ultrafiltrable form. This release of labelled materials is interpreted as the autolysis of cells killed by the chilling and centrifugation procedures employed. Certain of these labelled materials will be reassimilated by the surviving organisms unless large pools of unlabeled materials are added. The study of artificial death of cells by these standard laboratory techniques allowed the design of experiments to show that death under suitable growth conditions is in fact uncommon."

SHIBA, S., TERAWAKI, A., TAGUCHI, T. & KAWAMATA, J. **Selective Inhibition of Formation of Deoxyribonucleic Acid in *Escherichia coli* by Mitomycin C.** [Correspondence.] *Nature.* 1959, Apr. 11, v. 183, 1056–7.

ROCHE, J., SALVATORE, G. & FALCONE, G. Action des hormones thyroïdiennes et de l'acide 3 : 5 : 3'-triiodothyroacétique sur la respiration d'*Escherichia coli.* [**Action of Thyroid Hormones and 3 : 5 : 3'-Triiodothyroacetic Acid on the Respiration of *Escherichia coli*] *C.R. Soc. Biol.* 1959, v. 153, No. 2, 248–52, 1 fig. [12 refs.]

MORRIS, J. G. & WOODS, D. D. **Inter-Relationships of Serine, Glycine and Vitamin B_6 in the Growth of Mutants of *Escherichia coli.*** *J. General Microbiol.* 1959, June, v. 20, No. 3, 576–96, 11 figs. [40 refs.]

MORRIS, J. G. **The Synthesis of Vitamin B_6 by some Mutant Strains of *Escherichia coli.*** *J. General Microbiol.* 1959, June, v. 20, No. 3, 597–604, 1 fig.

RYAN, F. J. & KIRITANI, K. **Effect of Temperature on Natural Mutation in *Escherichia coli.*** *J. General Microbiol.* 1959, June, v. 20, No. 3, 644–53, 3 figs. [28 refs.]

BILLEN, D. **Alterations in the Radiosensitivity of *Escherichia coli* through Modification of Cellular Macromolecular Components.** *Biochim. et Biophys. Acta.* 1959, July, v. 34, No. 1, 110–16, 2 figs. [19 refs.]

STEWART, D. J. **The Phenylalanine Test on Kligler's Iron Agar for the Identification of *Proteus.*** [Correspondence.] *Nature.* 1959, May 30, v. 183, 1537–8.

When Kligler's iron agar slopes are used in routine diagnosis the surface growth can be washed off with

0·5 ml. of 2% L-phenylalanine solution in 0·1 M-phosphate buffer at *p*H 7·4. The suspension is shaken for 10 minutes in a bijou bottle, 0·1 ml. 8% aqueous ferric chloride added, and the bottle reshaken for 30 seconds. An intense green colour indicates phenylpyruvic acid. [This method is similar to the microtest described by SHAW and CLARKE, this *Bulletin*, 1956, v. 31, 447. For those taxonomists who include the Providence group in the genus *Proteus*, the phenylalanine test is specific for the genus.] *S. T. Cowan*

MARKS, J. **A Simple Method for the Cultivation of Tubercle Bacilli.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, May, v. 18, 81–6.

Methods were reported by the International Union against Tuberculosis (*Bull. Internat. Union Tuberculosis*, 1955, v. 25, 89) and by NASSAU [this *Bulletin*, 1958, v. 33, 509] which were claimed to meet the need for a relatively simple technique for cultivating tubercle bacilli. The method described in this paper, however, is considered to have advantages over both of these.

In this method 2 ml. of sputum is added by means of a sterile plugged glass tube to 2 ml. of 4% NaOH in a 1 oz. Universal container, care being taken to avoid contact with the upper half of the bottle. (If there is less than 2 ml. of sputum, water is added to make up the volume.) The containers are incubated at 37°C. and shaken for 20 seconds every 7½ minutes until the contents become watery; the maximum time of incubation was 22½ minutes.

The inocula which consisted of either 0·2 or 0·4 ml. were taken up into specially graduated pieces of glass tubing, 4 mm. in diameter and placed without neutralization on to the surface of an acid-egg medium and into an acid-fluid medium as soon as the specimens became watery. During the first week of incubation the egg medium was incubated with its surface horizontal.

Details of preparing the 2 media are given. The egg medium consists of KH_2PO_4, $MgSO_4$, glycerol, potato starch, malachite green, penicillin and fresh eggs; the fluid medium contains KH_2PO_4, Na_2HPO_4, $MgSO_4$, sodium citrate, glycerol, phenol red and tryptone (a pancreatic digest of casein, for which asparagine can be used as an alternative).

From the results of a comparative trial, in which some 2,000 specimens were examined, this method proved 99% as effective with film-positive specimens and 98% with film-negative specimens as the more elaborate method of MARKS and THOMAS [*ibid.*, 1959, v. 34, 159], in which the specimens are centrifuged and inoculated on to a buffered egg medium. *S. R. M. Bushby*

HIRSCH, A. & CATTANEO, C. Sulla differenziazione dei ceppi micobatterici per mezzo di un terreno contenente 2,3,5-trifenil-tetrazolio-cloruro. [**The identification of *Mycobacterium* strains by means of a 2,3,5-triphenyl-tetrazolium-chloride medium**] *Nuovi Ann. d'Igiene e Microbiol.* 1959, Jan.–Feb., v. 10, No. 1, 46–61, 2 figs. (1 coloured on pl.). [21 refs.] English summary.

An important objective in studies on mycobacteria is the possibility of identifying some chemical factor in their constitution which could be linked in an absolute sense with pathogenicity. This paper is a study of a reaction carried out through triphenyl-tetrazolium chloride, which, when reduced by bacterial growth, produces a coloured derivative which accumulates in the cell. The investigation was carried out on 37 strains belonging to 11 species, representing pathogens and non-pathogens. Herrold's medium (agar 31 gm., glycerin 12 ml., water 1,000 ml., and 1 egg yolk for every 100 ml.), containing triphenyl-tetrazolium chloride at a concentration of 10 mgm.%, was found to be the best giving identifiable colonies 2 to 3 days after being seeded from a culture. This medium turns red if exposed to direct strong sunlight, but this never occurs through indirect or artificial lighting. Pathogens produced pale pink colonies, saprophytes a bright red, with intermediate shades according to the species. [In a plate showing the growth on Petri dishes the identifying letters appear to be the wrong way round.] The method was not satisfactory when applied to mixed cultures or when pathological material was used as inoculum, though some way of using it in the latter connexion might be devised.

The extent of reduction of tetrazolium salts, leading to the formation of formazan, is linked with the varying metabolism of different species. Formazan persists in the cell, being insoluble and unassimilable, and can be observed by the electron microscope. Results obtained by using tetrazolium media agree with those of *in vitro* tetrazolium tests and virulence tests. *E. Agius*

DEGOMMIER, J. Flourescence et acido-alcoolo-résistance relative du bacille tuberculeux. [**Fluorescence and Relative Acid-Alcohol-Fastness of Tubercle Bacilli**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 723–33, 9 figs. [19 refs.]

In an examination of 1,209 pathological specimens for tubercle bacilli the films were examined first by fluorescence microscopy, fields which contained fluorescent bacilli being marked, so that when restained by the Ziehl-Neelsen method the same fields could be re-examined. In 15 of the 198 slides which were positive by fluorescence microscopy the bacilli were not seen in the Ziehl-Neelsen-stained films [see this *Bulletin*, 1958, v. 33, 167].

In an attempt to account for this discrepancy the author doubly stained smears of cultures of tubercle bacilli, of various ages, grown in Dubos or Youmans media or on Löwenstein-Jensen medium. The smears were first stained by the Ziehl-Neelsen method, decolourized with sulphuric acid and then ethanol, and then stained with auramine, acid alcohol being used for decolourizing. Microscopic fields of these doubly stained smears were first examined with white light and then with blue light, produced by raising the intensity of the lamp and the insertion of a filter.

Bacilli which stained deeply by the fuchsin were found not to fluoresce, while bacilli which stained feebly fluoresced moderately. Many bacilli were also found which fluoresced but did not stain with the fuchsin and as these were mainly in cultures showing active

multiplication, the author infers that it is the young tubercle bacilli that are detected only by fluorescence microscopy. *S. R. M. Bushby*

KUMASHIRO, A. **Studies on the Susceptibility of Rats to Various Strains of Mycobacteria. Report I. Growth of Mycobacteria in Rats and Gross Organ Changes.** *Acta Tuberculosea Japonica.* 1958, Dec., v. 8, Nos. 1/2, 1–9, 5 figs. [12 refs.] **Report II. Histological Examination of Rats infected with Various Strains of Mycobacteria.** *Ibid.*, 10–21, 8 figs. **Report III. The Humoral Defensive Power of Rats against Mycobacteria.** *Ibid.*, 22–31, 5 figs. [12 refs.]

FITZPATRICK, Florence K. **Studies with Kanamycin against** *Mycobacterium tuberculosis. Canadian J. Microbiol.* Ottawa. 1959, June, v. 5, No. 3, 305–9.

Tested in Dubos medium, 7 samples of Kanamycin A and 10 samples of Kanamycin A + B at concentrations of 0·078—0·156 μgm./ml. inhibited the growth of H37Rv and variants resistant to streptomycin and isoniazid, but showed no activity at 500 μgm./ml. against a neomycin-resistant variant; the bactericidal concentrations were about a quarter of these inhibitory concentrations. 3 samples of Kanamycin B were about 4 times less active against these strains. Against 2 chromogenic strains Kanamycin was about 20 times more active than streptomycin.

No evidence was found *in vitro* of synergism between this antibiotic and streptomycin, PAS or isoniazid. H37Rv developed resistance to Kanamycin less readily than to streptomycin, the increase in the minimum inhibitory concentration being only 4-fold after 10 successive passages.

In mice infected intravenously with H37Rv, 2 mgm. Kanamycin A + B, subcutaneously each day, increased the average survival time by more than 20 days and 1 mgm. increased it by 9·5–>20 days. Kanamycin A was almost as effective as the mixture but Kanamycin B was ineffective. In this experiment, in which untreated mice died in 18–20 days, the increase in survival time was 14–19 and 5–9 days by treatment with 2 and 1 mgm. streptomycin, respectively, per day, and 11 and 7 days by 2 and 1 mgm. neomycin, respectively, per day. Kanamycin also protected against streptomycin-resistant and isoniazid-resistant variants of H37Rv.

In combination, when sub-maximum effective doses were used, streptomycin, dihydrostreptomycin or neomycin showed a synergic effect in this infection when combined with Kanamycin, but isoniazid, PAS or pyrazinamide, in similar doses showed only an additive effect with Kanamycin. *S. R. M. Bushby*

HOWARD, J. G., BIOZZI, G., HALPERN, B. N., STIFFEL, C. & MOUTON, D. **The Effect of** *Mycobacterium tuberculosis* **(BCG) Infection on the Resistance of Mice to Bacterial Endotoxin and** *Salmonella enteritidis* **Infection.** *Brit. J. Exper. Path.* 1959, June, v. 40, No. 3, 281–90, 4 figs. [25 refs.]

The phagocytic activity of the reticulo-endothelial system of mice has been shown to be significantly stimulated when these animals are infected with the BCG strain of tubercle bacillus (BIOZZI *et al., Ann. Inst. Pasteur,* 1954, v. 87, 291). Mice infected with BCG 14 days previously were injected with a standard dose of colloidal carbon (16 mgm./100 gm.) and it was found that the blood stream clearance rate of this material by the reticulo-endothelial system was 5 times greater in the treated animals than in the controls.

On the other hand BCG treatment appeared to increase very significantly the susceptibility of mice to endotoxins (heat-killed saline suspension of *Salmonella typhi* and a purified lipopolysaccharide from *Escherichia coli*), although with ^{32}P-labelled lipopolysaccharide 71% was found to have been removed from the circulation 10 minutes after its administration in the BCG-treated mice as compared with 50% in the control animals. Notwithstanding the increased susceptibility of BCG-treated mice to *Salm. typhi* endotoxin, such mice were found to be more resistant than the controls to infection with small doses (1,000 bacteria) of living cultures of *Salm. enteritidis* as measured by mean survival time. The duration of the bacteraemia was also shorter.

The significance of these interesting observations seems rather involved at present and a clearer picture may emerge after further studies. *H. J. Bensted*

SCHWABACHER, Herta. **A Strain of** *Mycobacterium* **isolated from Skin Lesions of a Cold-Blooded Animal,** *Xenopus laevis,* **and its relation to Atypical Acid-Fast Bacilli occurring in Man.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 57–67, 7 figs. on 2 pls. [20 refs.]

This strain which the author has named *Mycobacterium xenopei* was grown from an adult female *Xenopus laevis.* When first observed, the toad had a brown nodular lesion on its back about 3 mm. in diameter and 2 small similar lesions on the dorsal surface of each thigh, but 3 days later 12 small blisters appeared on the back and sides of the animal. When the animal was killed 3 months later, the viscera were found to be normal.

The organisms from blister fluid grew slowly on Löwenstein-Jensen medium at 37°C. but not at 24°C. Mice, a guineapig and a rabbit could be infected, but not a hen.

Infected guineapigs and one rabbit were slightly sensitive to tuberculin and a similar preparation ("acidfastin") prepared from the organism, and there was some cross reaction by the haemoglobin test with antisera to human, bovine and especially to avian antisera.

The author compares in tabular form the cultural characteristics of the tubercle bacillus, *Myco. ulcerans, Myco. balnei, Myco. xenopei* and the saprophytes, and in the discussion she suggests that the chromogenic acid-fast bacilli cultured from skin lesions belong to the group of "Saprophytic acid-fast bacilli". The failure of this strain of *Myco. xenopei* to grow at 24°C. yet to be cultured from a cold-blooded animal is cited as evidence of the power of adaptation of these acid-fast bacilli. *S. R. M. Bushby*

ARONSON, J. D. & KRAUS, W. **The Correlation of the Reaction to Protein from certain Mycobacteria (Paratubercle Bacilli) with the Reaction to Tuberculin (OT).** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 731–7. [16 refs.]

"The results of this study indicate that the protein fractions from cultures of certain 'paratubercle bacilli' isolated from pulmonary lesions show marked variations in their antigenicity, varying from zero per cent to 96.0 per cent positive reactions. The thermostability of the skin-reacting material varies with the different mycobacteria.

"The results of simultaneous tests made with Old Tuberculin and protein from different 'paratubercle bacilli' indicate some common antigenic relationship between typical tubercle bacilli and certain of the 'paratubercle bacilli,' including some chromogenic mycobacteria."

MORRIS, J. A. & NAKAMURA, K. **Behavior of Human Leprosy Bacilli in Cultures of Human Cells.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 73–5.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1139.]

BERGEL, M. **Influence of Various Pro-Oxidant Nutritional Conditions on the Growth** *in vivo* **of** *M. leprae. Leprosy Review.* 1959, July, v. 30, No. 3, 153–8, 4 figs. on 2 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1139.]

OOTAKA, K., SATOO, S., SATOO, J. & MIURA, N. Une nouvelle coloration différentielle entre les bacilles de la tuberculose et les bacilles de la lèpre. [**A New Method of Differential Staining between the Bacilli of Tuberculosis and the Bacilli of Leprosy**] *Hirosaki Med. J.* 1959, Mar. 25, v. 10, No. 2, *67–*70.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1140.]

HILL, L. R. **The Adansonian Classification of the Staphylococci.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 277–83, 2 figs. [17 refs.]

49 strains of staphylococci from nasal swabs, septic lesions, milk, air, the National Collection of Type Cultures, etc. were examined by 39 tests to give a total of 80 features. The similarities between the strains were then tested by SNEATH's method [this *Bulletin*, 1957, v. 32, 1181]. 3 reasonably well-defined "species" could be distinguished, corresponding to those described by SHAW, STITT & COWAN [this *Bulletin*, 1952, v. 27, 484] as *Staphylococcus aureus, saprophyticus* and *roseus.* The first 2 are more closely similar to one another than to the last and it is suggested that the genetic name *Staphylococcus* might be reserved for them, leaving *Micrococcus* for the *roseus* strains. *Staph. aureus* was distinguished from *Staph. saprophyticus* by pigment, coagulase and α-lysin production. The distinction of *Staph saprophyticus* from the miscellaneous micrococci, which constituted 21 of the strains tested, is not explicitly set out. *R. E. O. Williams*

HARRISON, K. Joy, BEAVON, Jane & GRIFFIN, E. **The Effect of Neomycin on Phage-Typing of Staphylococci.** *Lancet.* 1959, May 2, 908–10, 1 fig.

The recovery of strains of staphylococci not lysed by phage 80 from noses of previous carriers of type 80 strains after local treatment with a mixture of neomycin sulphate 0·25% and Tyrothricin 0·02%, suggested to the authors that the strains might have become temporarily resistant to that phage. A strain of type 80 was therefore grown in dilutions of the neomycin-tyrothricin solution from 1 in 10 to 1 in 100,000. After 24 hours' incubation, growth was moderate in 1 in 1,000 and 1 in 1,250 dilutions and heavy in dilutions above 1 in 1,500. A loopful of culture from all tubes showing growth was transferred to tryptone agar plates enriched with aneurine and nicotinamide and a drop of phage 80 at routine test dose was applied. There was no lysis of organisms from 1 in 1,000 and 1 in 1,250 and only partial lysis of organisms from 1 in 1,500 and 1 in 4,000 dilution tubes. [Growth from all tubes was apparently good.] After 3 subcultures in serum broth strains had regained their sensitivity to phage 80.

Similar experiments with 19 routine hospital strains which were lysed by phages 80 and 52 gave the same results: phage sensitivity was lost when tested from the highest concentration of drug permitting growth. This loss occurred after growth in neomycin only, and was accompanied by depression of alpha-lysin production. No loss of phage sensitivity occurred with Tyrothricin or chloramphenicol. *M. Patricia Jevons*

TAPLIN, Jennifer & GOLDSWORTHY, N. E. **A Comparison of Strains of** *Staphylococcus* **isolated from the Mouth of Two Different Groups of Children.** *Med. J. Australia.* 1959, Feb. 21, v. 1, No. 8, 259–63. [15 refs.]

Saliva samples were collected from 65 children in a residential institution in Sydney and from 65 children from the general population of the city. Cultures of these specimens yielded respectively 111 and 114 cultures of staphylococci, which were submitted to a large number of physiological tests [see this *Bulletin*, 1959, v. 34, 491] details of which must be sought in the original. 64 of the strains from the institution children were coagulase-positive, but only 15 of those from the general population; 15 of the former were penicillin-resistant but none of the latter. Phage typing failed to reveal a dominant strain among the institution children but suggested that some might have acquired their staphylococci from milk. [The small number of strains, and the method of selection of the colonies, make useful assessment of the results difficult.]

R. E. O. Williams

HUNT, G. A. & MOSES, A. J. **Acute Infection of Mice with Smith Strain of** *Staphylococcus aureus. Science.* 1958, Dec. 19, v. 128, 1574–5.

The Smith strain of *Staphylococcus aureus* (see SMITH & DUBOS, *J. Exper. Med.*, 1956, v. 103, 87 [this *Bulletin*,

1956, v. 31, 673]) when grown in soft agar containing plasma, produced compact and diffuse colonies. The compact-colony form was agglutinated by COWAN type II antiserum and was susceptible to phage 44A; the diffuse-colony form was not. The diffuse-colony form was virulent for mice, and was able to multiply within mouse leucocytes; the compact-colony form was engulfed by leucocytes, but did not multiply within them.

R. E. O. Williams

NORTH, E. A. **Adverse Effect of Filtration on the Immunizing Power of Staphylococcal Toxin and Toxoid.** *Australian J. Exper. Biol. & Med. Sci.* 1958, Dec., v. 36, Pt. 6, 547–54.

Staphylococcal toxin or toxoid, prepared from crude culture supernatants, was used to immunize mice, which were later challenged with a dose of about $1{\cdot}5 \times 10^8$ living staphylococci suspended in a mixture of 1% human fibrinogen and 1% human plasma in saline.

Unfiltered toxin always gave better protection than toxin that had been filtered through a Seitz pad; filtration through sintered glass or a membrane filter had less deleterious effect. Filtered toxin also had less haemolytic activity and a lower combining power than unfiltered. Filtration of toxoid also led to loss of ability to induce protection; it did not however greatly reduce its ability to induce production of antihaemolysin. [*Cf.* FISHER, this *Bulletin*, 1958, v. 33, 518.]

R. E. O. Williams

FISHER, M. W. **Measurement of a Staphylococcal Antibody in Human Serum by a Mouse Protection Test.** [Correspondence.] *Nature.* 1959, June 13, v. 183, 1692–3. [12 refs.]

The assay of a mouse-protecting antibody against a strain of staphylococcus is described.

Mice are challenged intraperitoneally with 10–20 LD50 of fresh cells of the Smith strain of *Staph. aureus* suspended in 0·5 ml. 5% hog gastric mucin. Within 30 minutes groups of 10 mice each are infected intraperitoneally with 0·25 ml. of serum dilutions 1/10, 1/100 and 1/1,000 and the 5-day survival values obtained. This titration serves as a guide for the definitive assay with 2-fold dilutions over the suitable range and 15–20 mice are used in each group. The PD50 [protective dilution] is calculated by the MILLER-TAINTER method (*Proc. Soc. Exper. Biol. & Med.*, 1944, v. 57, 261).

Assays were done using other staphylococcal strains as challenge strains but results are not given. PD50 titres of 50 normal adults' serum ranged from 1/3–1/2,000 with a geometric mean of 1/192 and the PD50 of a limited number of sera from patients with chronic staphylococcal lesions was low. [No details are given of the development of this antibody as a result of stimulation with the Smith or other strains of staphylococci, or of its specificity.] *M. Patricia Jevons*

MITCHELL, P. & MOYLE, Jennifer. **Permeability of the Envelopes of *Staphylococcus aureus* to some Salts, Amino Acids, and Non-Electrolytes.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 434–41, 4 figs. [11 refs.]

This paper collects together observations made upon the permeability of the envelopes of *Staphylococcus aureus* (strain Duncan). The word permeability is used as an index of the rate at which a given solute undergoes *net transport* through the plasma membrane under an electrochemical gradient.

The plasma membrane was studied by testing its function of retaining internal and excluding external solutes. The former was assessed from the internal osmotic pressure measured either by the osmotic pressure required to prevent swelling and lysis of protoplasts (cell-wall-free) [this *Bulletin*, 1957, v. 32, 621] or by a vapour pressure equilibrium method applicable to intact organisms. The function of the plasma membrane in excluding external solutes was assessed from the rate of penetration of solutes into the cells of a very thick suspension or by measurements of the rate of swelling and lysis of cell-wall-free protoplasts in solutions of the solute (*J. General Microbiol.* 1953, v. 9, 57, 273).

The vapour pressure equilibrium measurements show that the weight of water held in the organisms is proportional to the reciprocal of the osmotic pressure for values up to 1·8 gm. water/gm. dry weight of organisms. This corresponded to the osmotic pressure exerted by 1 Molal sucrose (or 20 to 25 atmospheres).

Above this value the weight of water held increased much more slowly with the reciprocal of the osmotic pressure of the equilibriating sucrose solutions. It was therefore concluded that the protoplast is prevented from swelling by the cell wall, which withstands a hydrostatic pressure of some 20–30 atmospheres exerted against it by the plasma membrane in distilled water.

Permeability measurements at 2°C. and 25°C. on thick suspensions were carried out with glutamate, glutamine, glycine, chloride, thiocyanate and a leuconostoc dextran of molecular weight 10,000. The corresponding phosphate-impermeable volumes were determined for comparison. Both solute and phosphate-impermeable volumes were also determined after breakage of the osmotic barrier with 5% butanol. Neither glutamine nor glutamate appeared to penetrate the cells during 30 minutes at 25°C. but some glutamine was probably adsorbed on the surface. Glycine was probably adsorbed but did not penetrate at 2°C.; at 25°C. it evidently passed through the membrane. At 2°C. chloride entered the cells slowly and thiocyanate rapidly; the latter anion did not damage the barrier sufficiently to cause leakage of phosphate. Normal and butanol-treated cocci were impermeable to the dextran, thus demonstrating that the osmotic barrier for phosphate and other small molecular weight solutes (" plasma membrane ") was not the same as that for the high molecular dextran (outer region of the cell wall). Permeability properties of protoplasts of *Staph. aureus* closely resembled those of the intact organisms.

H. Gooder

VAN DEN HOOFF, A. & HIJMANS, W. **An Electron Microscope Study of L Forms of Group A Streptococci.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 1, 88–96, 8 figs.

WOOD, H. F. & SCHRAMM, Hanna. **Precipitin Reaction Obtainable between Human Serum and Extracts of Group A, Type 15 Streptococci.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 870–72.

Sera from 100 patients with a recent history of rheumatic fever and from 35 controls were all found to give strong precipitin reactions when tested with group A extracts of 2 Type 15 streptococci containing M protein antigen, which is associated with virulence. Extracts, made from two glossy variants of T15 strains, gave no reactions when tested with the majority of sera and weak reactions with the remainder. Sera from 6 normal rabbits gave no precipitation with these extracts and no reactions were obtained when the human sera were tested with batches of media used to grow the strains.

The reacting substance in the T15 cells was like the M protein in that it was present in partially purified M extracts of cells and cell walls, it was trypsin sensitive and was absent from glossy variants of T15 strains.

The unknown reacting factor is not, however, thought to be M antigen since precipitin reactions between M extracts and convalescent sera from patients infected with the homologous strain are very rare or unknown, and infection with T15 streptococci is extremely uncommon. *M. Patricia Jevons*

HEYL, J. G. **On the Stability of Reduced Fluid Streptolysin O.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 1, 46–8.

"A method for preparing and storing reduced streptolysin O is described. The reliability of this method has been confirmed by the results of the titrations of different batches of reduced streptolysin O at different times after preparation."

LIAMPERT, I. M. **The Rapid Increase in the Resistance to the Erythrogenic Toxin of the Haemolytic** *Streptococcus* **after its Parenteral Injection.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 6, 893–900, 5 figs. [24 refs.] [Translated from Russian.]

After a brief review of the previous work illustrating the rapid increase in "resistance" to various antigen induced by the injection of the antigen, the author reports experiments in which rabbits were injected intravenously with 25,000 skin test doses (STD) of streptococcus erythrogenic toxin and 3 hours later were skin tested with 1–40 STD. Before the experiment, all rabbits reacted to 0·1 STD; after 3 hours 18 of 32 did not react even to 40 STD. The injected rabbits were also somewhat resistant to intravenous challenge with toxin. The resistance was in both cases greater than the antitoxic immunity induced by a single dose. Rabbits kept at temperatures below 0°C. for several days also showed increased resistance to intradermal injection of toxin. *R. E. O. Williams*

BERGER, U. Experimentelle Grundlagen zur Behandlung von Streptokokkeninfektionen mit Nitrofurazon. [**Investigations on the Treatment of Streptococcal Infections with Nitrofurazon**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 175–83. [29 refs.]

Findings on the action of nitrofurazone (5-nitro-2-furaldehyde semicarbazone) on haemolytic streptococci both *in vitro* and *in vivo* are conflicting. The author collected 103 strains of different Lancefield groups and determined the minimum inhibitory concentration of nitrofurazone for them by a tube dilution test in broth. 25 strains of Group A, 16 of C, 11 of F, 15 of G and a few of E, H, L and O were all inhibited by 50 μgm./ml. and most by lower concentrations. Almost all strains of Group B (18) and D (8) were uninhibited by 100 μgm./ml. The use of strains of different Lancefield groups may therefore account for these discordant findings. As a specific instance of this, the author protests against the use of the "Aronson mouse" (*i.e.* mice inoculated with the Aronson strain of *Streptococcus pyogenes*): this is said to be of Group B and consequently an unsuitable test organism as a guide to the treatment of human infections. *L. P. Garrod*

KAMAL, A. M. **Studies on the Cultivation of Brucella abortus in the Developing Chick Embryo. II. Study of an Egg-Passage Strain, Inoculation with Rough and Mucoid Forms, and Histology of Infected Tissues.** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 81–97, 8 figs.

Experiments with egg-to-egg transfer of *Brucella abortus* show that the organism can invade the cells of the 3 primary germ layers and may be found in practically all the internal organs—particularly the liver and kidney. This egg-to-egg transfer does not alter the colonial characters of an R-form or modify its serological reactions, but it does increase the virulence of the culture for the developing chick embryo and also for mice. Rough and mucoid forms of *Br. abortus* have a low virulence for their natural host and also for the normal laboratory experimental animals but they have a high virulence for the developing chick embryo. The serial egg passage does not induce a R–S change, nevertheless these cultures behave towards the developing chick embryo in the same way as virulent S-forms. *H. J. Bensted*

MARKENSON, J., SULITZEANU, D. & OLITZKI, A. L. **Immunizing properties of Insoluble Cell Material derived from** *Brucella.* [Correspondence.] *Nature.* 1959, June 13, v. 183, 1693.

The immunizing properties of 2 insoluble fractions obtained by sonic disintegration from *Brucella abortus* and *Br. suis* were studied. The sonic extract was centrifuged at 10,000 r.p.m. and the sediment freed from intact cells by differential centrifugation. The second fraction was obtained from the supernatant fluid left after the first centrifugation by spinning at 40,000 r.p.m. These were compared in mice with the activity of whole cells. Protection indices, calculated as the ratio of brucellae

in the spleens of normal and treated mice, were consistently markedly higher with the insoluble fractions, the smaller particle fraction, obtained after the more rapid centrifugation, appearing to be the more efficient. The insoluble fractions appear to be cell-wall fragments.

E. Agius

BRUMFITT, W. **Some Growth Requirements of *Haemophilus influenzae* and *Haemophilus pertussis*.** *J. Path. & Bact.* 1959, Jan., v. 77, No. 1, 95–100, 1 fig. [15 refs.]

The growth requirements of small inocula of *Haemophilus pertussis* and *H. influenzae* have been investigated by the addition of various growth factors to a basic medium of COHEN and WHEELER [this *Bulletin*, 1947, v. 22, 558] solidified by addition of 2% washed, defatted agar. Both species of organisms required either catalase or haematin for growth from small inocula, and neither was able to synthesize its porphyrin requirements from substances simpler than protoporphyrin IX, which was in itself much less efficient in promoting growth than haematin.

The essential difference between the two organisms is that for optimum growth of *H. pertussis* charcoal or other adsorbant was essential. *H. pertussis* grew well on chocolate agar when charcoal was added.

F. T. Perkins

LIN, Tong-Ming, LIU, Chia-Ho & WU, Yan-Ming. **Use of Blood- and Charcoal-Free Agar Medium for the Preparation of Pertussis Vaccine.** *J. Formosan Med. Ass.* 1959, Feb. 28, v. 58, No. 2, 43–9. [12 refs.]

"Blood- and charcoal-free agar medium (BCF medium) has been found suitable for the preparation of pertussis vaccine. The medium is easy to prepare and inexpensive and compensates the weak points of those media usually used for the preparation of the vaccine such as Bordet-Gengou medium, fluid medium and charcoal agar medium, and for these reasons it seems to be a medium of choice for the preparation of pertussis vaccine.

"Preparation of medium; To 1,000 ml. of Cohen Wheeler's fluid medium add 10 ml. glycerin, 12 g. proteose peptone (difco) and 25 g. agar. The medium, after melting and adjustment of pH to 7.2–7.3 was dispensed in 7 ml. amounts in 175 × 22 mm tubes and in 100 ml. amounts in 1,000 ml. culture flasks. Autoclave at 10 lb. pressure for 30 minutes."

BARBER, Cella & SOARE, Irina. Sur la composition chimique et antigénique du bacille *Haemophilus pertussis*. [**On the Chemical and Antigenic Structure of *Haemophilus pertussis***] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Mar., v. 17, No. 1, 119–24.

5 strains of *Haemophilus pertussis* showed a constant chemical composition when grown on a medium in which charcoal replaced blood. Changes in the composition of the culture medium resulted in variations occurring in both the lipid and ribonucleic acid content of the organisms.

Extraction of the organisms with 2·5 M urea gave a fraction which protected mice against intranasal infection with pertussis and produced high agglutinin titres in them. Treatment of the organisms with N/4 HCl. at 80°C. for 40 minutes extracted a polysaccharide which is non-toxic and does not give necrosis when injected intradermally into a guineapig. This extract has been tried in a limited number of human volunteers to assess its usefulness in the diagnosis of whooping cough.

F. T. Perkins

POZSGI, N., FAUR, Yvonne & ANDREESCO-TIGOIU, Viorica. Quelques aspects de variabilité dirigée chez l'*Haemophillus pertussis*. [**Some Aspects of Directed Variability in *Haemophilus pertussis***] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 255–70, 16 figs. [13 refs.]

The appearance of colonies of *Haemophilus pertussis* isolated from infected mice were found to be dependent on the medium used for isolation and the immune state of the mouse from which they were isolated.

The morphological appearance of the organisms from all different colonies was always coccoidal but the organisms isolated from peritoneal fluid after infection of vaccinated mice showed large globular forms. The authors believe that these globular forms may be considered to be L forms, but their attempts to produce "filterable" forms of pertussis have been unsuccessful.

F. T. Perkins

LIN, Tong-Ming. **Experimental Whooping Cough in Monkey.** *J. Formosan Med. Ass.* 1958, Aug. 28, v. 57, No. 8, 505–14. [13 refs.]

Spraying a bacterial suspension of a phase 1 strain of *Bordetella pertussis* intranasally was successful in establishing whooping-cough in monkeys. It was also possible to transmit a natural infection by caging a normal with an infected monkey. The course of the disease and period of paroxysmal stage in monkeys were shorter than in human cases.

It was found that the severity of the infection was not correlated with the virulence of the strains for mice or with the ability of the strain to give a rapid agglutination with antisera. Monkeys surviving the infection were immune to subsequent infections although the opsonic index and agglutin titre of their sera were low after a single attack. Infection with the Sakairi strain (a type III strain) which did not give clinical whooping-cough, nevertheless protected monkeys against infection with a virulent strain and in these animals a carrier state was demonstrated.

F. T. Perkins

DOLBY, Jean M. **The Separation of the Histamine-Sensitizing Factor from the Protective Antigens of *Bordetella pertussis*.** *Immunology*. Oxford. 1958, Oct., v. 1, No. 4, 328–37, 1 fig. [26 refs.]

Tests on fractions extracted from *Bordetella* [*Haemophilus*] *pertussis* have shown the histamine-sensitizing

factor to be different from the antigen protecting mice against an intracerebral challenge. Broken cells were extracted with calcium chloride and the extract treated with 10% methanol. The resulting precipitate was a water-soluble fraction which contained the histamine-sensitizing factor and the antigen protecting mice against intracerebral challenge. Dialysis of this fraction yields a precipitate soluble at *p*H 7, containing a much greater amount of protective antigen than histamine-sensitizing factor and supernatant which has high histamine-sensitizing activity and is of poor immunizing potency.

Antisera to the material precipitated on dialysis are fairly specific, protecting against an intracerebral challenge but not against an intranasal challenge, and they do not contain antihistamine-sensitizing factor. The supernatant is much less pure; it stimulates antibodies to the histamine-sensitizing factor and also contains both protective antigens. Sera to other fractions have been obtained, however, which protect against an intranasal challenge but do not contain anti-histamine-sensitizing factor.

Although mixtures of antigens and mixtures of antibodies were used, sufficient evidence was obtained to distinguish the histamine-sensitizing factor from the two types of protective antigen.

The histamine-sensitizing factor is distinct from the agglutinogen, the haemagglutin and the toxin.

F. T. Perkins

NIWA, M., YAMADEYA, Y., MATSUI, T. & KUWAJIMA, Y.; MATSUI, T., KISHIGAMI, M. & KUWAJIMA, Y. **Reduced Activity of Histaminase in Rats sensitized by** *Bordetella pertussis*. [Correspondence.] *Nature*. 1959, Mar. 14, v. 183, 755–6.

The histaminase activity of the lungs of rats taken 5 days after sensitization with a single intraperitoneal dose of a supernatant fluid from a pertussis culture was found to be less than that of the lungs from uninoculated rats. No histaminase activity could be detected in tissues other than the lungs and liver.

In an additional note the authors report that the liver and brain of sensitized mice showed a lower histamine-inactivating activity than those of non-sensitized mice. *F. T. Perkins*

KUWAJIMA, Y., MATSUI, T., NAKA, K. & KANAI, Y. **Inability of Pertussis Toxin to act as Preventive Antigen in Experimental Mouse Infection of** *Bordetella pertussis*. *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 274–84, 3 figs. (2 on pl.) [22 refs.]

Using a particular phase III strain of *Bordetella* [*Haemophilus*] *pertussis* which had a common thermolabile L antigen with phase I but had no phase I thermostable K antigen, the authors showed that injection of the live organisms produced in rabbits an antitoxin that had serological crossing with toxin produced by a phase I organism. Active or passive immunization of mice with these phase III organisms did not give any protection against intracerebral challenge, although they did sensitize the mice to histamine. *F. T. Perkins*

KRATOCHVÍLOVÁ, V., JELÍNEK, J. & RASKA, K. **Vaccination during the Incubation Period. II. A Comparison of Intranasal and Intracerebral Infection with** *H. pertussis*. *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 1, 23–8, 2 graphs.

The authors have studied the effect of challenging mice either intranasally or intracerebrally within a short period of immunization with a single intraperitoneal dose of pertussis vaccine. With intranasal challenge, a rise in death rate occurred not only if the mice were vaccinated after the challenge dose but also if they were vaccinated 5 or 24 hours before challenge. With intracerebral challenge, vaccination had a protective effect if it preceded the challenge by more than 5 hours and if the mice were challenged within 5 hours of immunization a slightly higher death rate occurred.

The authors believe that there was less variability in their results after intranasal than after intracerebral challenge and therefore recommend the former route for standardization of vaccines. *F. T. Perkins*

YAMAMOTO, A. *et al.* **Studies on the** *Haemophilus pertussis*. **XI. On Antitoxic Tissue Immunity.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 217–23, 3 figs.

Guineapigs were given 5 intracutaneous injections at 5-day intervals of either a commercial pertussis vaccine or a vaccine made from a *Haemophilus pertussis* type O strain which had lost its toxicity as well as its capsular material. These guineapigs, together with those of unimmunized controls, were afterwards injected intracutaneously with 1 ml. of crude pertussis toxin and 24 hours later intradermal reactions were read. The animals were then sacrificed and the tissue reaction in the lungs observed by histological methods.

An interstitial pneumonic reaction occurred in the lungs of the control animals and also in those injected with the type O vaccine. This tissue reaction did not occur in the guineapigs immunized with commercial vaccine.

From these observations the authors conclude that some antitoxic immunity occurred in the lungs of immunized guineapigs. *F. T. Perkins*

SATO, M. **Studies on the Fractionation of** *Haemophilus pertussis* **Antitoxin.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 279–84, 4 figs.

Antitoxic serum containing no agglutinins was produced by immunizing rabbits with a non-purified pertussis toxoid and absorbing the serum with *Haemophilus pertussis* organisms. Fractionation of this serum by zone electrophoresis showed the antitoxin to be a gamma globulin which was electrophoretically homogeneous. The purified antitoxin which contained no agglutinin had not lost titre during purification; it was shown to be ineffective in protecting mice against death when challenged with an intracerebral injection of pertussis organisms. *F. T. Perkins*

Sato, M., Tenjin, H. & Iida, T. **Fractionation of *Haemophilus pertussis* Antiserum Proteins.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 309–16, 2 figs. [13 refs.]

Fractionation of serum from rabbits which had been given a series of injections of some extract of pertussis phase I organisms showed that the agglutinins, antitoxin and mouse-protective antibody could not be separated by chemical and physical methods. Zone electrophoresis showed that all three antibodies were in the gamma globulin fraction.

Fractionation of pertussis immune horse serum by cold ethanol or zone electrophoresis showed that the agglutinins were concentrated in both the beta and $gamma_2$ globulins and the antitoxin in the $gamma_2$ globulins. Mouse protective antibody could not be measured quantitatively. *F. T. Perkins*

Kasuga, T., Ukishima, K. & Nakase, Y. **Antigenic Structure and Phases of *Hemophilus parapertussis*.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 231–40. [10 refs.]

Agglutination reactions have been used to determine the antigenic structure and phase variations of *Haemophilus parapertussis*. There are 3 antigenic phases which have the following structure:—

Antigen	Phase I	Phase III_1	Phase III_2
Capsular thermolabile L	+	−	−
Capsular thermostable S	+	−	−
Pathogenicity	+	−	−
Haemagglutinin	+	−	−
Toxin	+	−	−
Protective	+	−	−
Thermostable O antigen 2	+	+	−
O antigen 3	−	+	+

Variations occur from phase I to phase III_1 and from phase III_1 to phase III_2. *F. T. Perkins*

Gastinel, P., Collart, P. & Dunoyer, F. Étude sur le comportement du tréponème de Reiter en milieu pénicilliné. [**Behaviour of Reiter's *Treponema* in Penicillin-containing Media**] *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 381–401, 7 figs. [16 refs.]

This is a somewhat discursive account of experiments in which the Reiter strain of treponema was cultivated in Brewer's medium with added horse serum and containing different concentrations of penicillin, the usual period of incubation being 8 days. The minimum inhibitory concentration was about 0·15 unit/ml., but after more prolonged incubation growth eventually appeared in somewhat higher concentrations. After 15 such transfers there was no acquired resistance in the ordinary sense, but a state of "tolerance" developed, enabling the organism to grow without delay in concentrations which delayed the growth of a previously unexposed culture by many days. A similar effect resulted from shorter exposure to higher concentrations. The results of an attempt to determine whether this tolerance is lost during further transfers in normal medium were somewhat conflicting. Some observations were also made on the effects of exposure to much higher concentrations and on the morphological changes produced, which are illustrated. It is emphasized that treponemes rendered non-motile are not necessarily dead. *L. P. Garrod*

Mutermilch, S., Gérard, S. & Delaville, M. Contribution à l'étude du tréponème de Reiter. [**Contribution to the Study of Reiter's *Treponema***] *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 402–12. [10 refs.]

This paper gives the results of experiments of 3 different kinds, but all employing cultures of the Reiter treponema in Brewer's medium. In the first series, very briefly described, successive transfers were made in medium containing penicillin, chloramphenicol or chlortetracycline: no increase in resistance to any of these antibiotics was obtained. Some observations were also made in this connexion on the effect of penicillin on the morphology of the organism, and the changes observed resembled those seen in aging cultures. Secondly, in pursuance of a finding by other workers that an extract of liver enhances the action of anti-syphilitic drugs *in vitro*, parts of organs from a rabbit which had been given a large dose of penicillin the day before were added to cultures: liver produced rapid immobilization, spleen a similar delayed effect, and kidney and serum had no effect. The effect of normal liver and penicillin added separately was similar but less marked. Finally determinations were made of the minimum inhibitory concentrations of salts of mercury, arsenic, bismuth, gold and vanadium, and the results are said to tally with the known relative therapeutic activities of these substances in syphilis. *L. P. Garrod*

Girard, G. Sur la production de concrétions cristallomorphes de nature protidique par une souche de *Pasteurella pestis*. [**Production of Crystalline Concretions of a Protein Nature by a Strain of *Pasteurella pestis***] *C.R. Soc. Biol.* 1959, v. 153, No. 2, 277–9.

Manigault, P. Observation au microscope des productions cristallines de la souche *Pasteurella pestis* EV (Girard et Robic). [**Microscopic Observations on the Crystalline Concretions Produced by *Pasteurella pestis*, Strain EV**] *Ibid.*, 279–80, 1 fig.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1128.]

Dodin, A. & Brygoo, E. R. I. Activité succinodeshydrogenasique de *Pasteurella pestis*, souche E. V. I. Étude colorimetrique. [**Succinodehydrogenase Activity of *P. pestis*, Strain EV. I. Colorimetric Study**] *Arch. Inst. Pasteur de Madagascar.* 1959, v. 27, 13–16, 2 graphs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1128.]

MUKERJEE, S. **Identification of S-R Dissociation of the Strains of *Vibrio cholerae* by Group II Bacteriophages.** *Ann. Biochem. & Exper. Med.* 1959, Jan., v. 19, No. 1, 9–12, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1130.]

LIU, P. V. **Studies on the Hemolysin of *Vibrio cholerae*.** *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 238–52, 11 figs. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1131.]

TAKAISHI, K. [**Morphological and Immunochemical Studies on the Cell Wall of *Vibrio cholerae***] *Shikoku Acta Med.* 1959, Mar., v. 14, No. 3, 354–81, 8 pls. & 2 figs. [81 refs.] [In Japanese.] English summary.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1131.]

MUKHERJI, A. **Toxin Production and Virulence of Inaba and Ogawa Vibrios.** *J. Immunology.* 1959, May, v. 82, No. 5, 381–4. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v 56, 1132.]

FUNGI

GRIGORAKI, L. Les bases d'un accord entre dermatologistes et mycologues sur une classification unique des dermatophytes. [**Basis of Agreement between Dermatologists and Mycologists Regarding a Single Classification of Dermatophytes**] *Mycopathologia.* The Hague. 1959, May 30, v. 10, No. 4, 317–40. [Numerous refs.]

GRIN, E. I. Upliv zemlje i njezine mikropopulacije na patogene dermatofite u inficiranoj dlaci. [**Influence of Soil and its Micropopulation on Pathogenic Dermatophytes in Parasitized Hair**] Reprinted from *Nauč Društvo nr Bosne i Hercegovine.* Sarajevo. 1959, v. 12, 1–22, 13 figs. on 7 pls. [26 refs.] English summary.

Hairs infected by *Trichophyton violaceum* when placed in moistened unsterilized soil provided evidence of antifungal activity by soil micro-organisms in so far as the fungal elements in the hair gradually lost their shape and completely disintegrated into a granular mass in a period of 6–8 days. Notwithstanding this, the keratin of the hair appeared to be unaffected. This result was obtained irrespectively of the type of soil used.

Attempts to isolate the organisms responsible for the breakdown of the fungus pathogen in the hair by means of Imsenecki's culture medium and filter-paper method as well as conventional culture media, resulted in the isolation of a number of cellulose bacteria belonging to Winogradsky's "cellvibrions". Experiments also revealed that the microbial population (presumably bacteria) introduced with the hair into the soil was also capable of decomposing the dermatophyte within the hair.

The author concludes from this evidence that dermatophytes such as *T. violaceum* which have become specially adapted to parasitic life in the human hair are not likely to be able to maintain an independent saprophytic existence in the soil.

C. J. La Touche

EDWARDS, G. A., EDWARDS, M. R. & HAZEN, Elizabeth L. **Electron Microscopic Study of Histoplasma in Mouse Spleen.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 429–38, 8 figs. on 4 pls. [33 refs.]

This study of two strains of *Histoplasma capsulatum* and one of *H. duboisii* in the spleens of experimentally inoculated mice has revealed some interesting cytological features in these two species as well as in the tissue of the host.

Although the yeast phase of *H. duboisii* averages 5·5 times the size of the yeast phase of *H. capsulatum* in mouse spleen, in its fine structure it is similar in both species. Moreover, examination by electron microscopy has not only enabled the authors to confirm the fact previously disclosed by several other workers [see, for example, this *Bulletin*, 1956, v. 31, 588] that the clear zone around the yeast-like cells seen in the host cell is not a capsule, but has enabled them as well to observe in these cells such protoplasmic details as:— plasma membrane, a cytoplasmic matrix, mitochondria, a reticulum and a Golgi complex. The nucleus is also fully differentiated and the cell wall varies in thickness and lamination.

These features are well illustrated in a series of excellent photographs. Host reactions to the presence of these fungal parasites include various degenerative changes which contribute to the formation of the clear zone around the *Histoplasma* cells and also the formation of various intracytoplasmic bodies of unknown nature.

C. J. La Touche

EDWARDS, Mercedes R., HAZEN, Elizabeth L. & EDWARDS, G. A. **The Fine Structure of the Yeast-Like Cells of *Histoplasma* in Culture.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 496–503, 19 figs. on 6 pls. [34 refs.]

BLYTH, W. **Host/Parasite Relationship in Experimental Moniliasis: 1. *Candida albicans*.** *Mycopathologia.* The Hague. 1959, May 30, v. 10, No. 4, 269–82, 8 figs. [19 refs.]

In order to test the pathogenicity of a number of isolates of *Candida albicans* obtained from various sources, *e.g.* vagina, appendix, sputum, etc., the author inoculated batches of mice intraperitoneally with a suspension of the organism in amounts of 0·2 ml. containing 1,000,000–1,200,000 blastospores. He also tested the effect of diminishing blastospore densities on further

batches of mice. These experiments showed that certain of the isolates were not pathogenic and that the range of survival of the mice inoculated with the pathogenic isolates tended to increase inversely with the density of the inoculum.

Clinical symptoms exhibited by inoculated mice included lethargy, emaciation and excessive thirst. The pathological response to infection was of 2 types; acute in the case of animals dying within 12 days from the date of inoculation; chronic in the case of animals which survived beyond 12 days from the date of inoculation. As the length of survival of the mice was found to be correlated with the degree of involvement of the kidney, particular attention was paid to the histopathology and host-parasite relationship in this organ. In the acute form of the disease, numerous abscesses and, frequently, granulomata, were present in the cortex, and a few in the medulla, and there was minimal fungal invasion of the pelvis. In the chronic form of the disease, abscesses and granulomata were generally absent from the cortex, while the invasive process was particularly marked in the pelvis.

The morphology of the fungus presented 3 different phases according to different host-tissue response. These were, according to the author: 1. "In areas in which no specific host defence reaction is evident, a fine pseudomycelium of predominantly monaxial growth potential with elongate elements;" 2. "where the basic pseudomycelium encounters an inflammatory exudate . . . a transitional mycelium of restricted polar growth, deeply constricted into short elements and subject to intense verticillation, then appears;" 3. "Decrease in fungal growth appears to occur when necrosis of polymorphs and host tissue takes place. It is indicated firstly by degeneration and fragmentation of some fungal elements, and secondly by the appearance of distinct septation followed by enlargement and extreme vacuolation of the cells so delimited".

C. J. La Touche

BACTERIOPHAGES

Uetake, H., Luria, S. E. & Burrous, J. W. **Conversion of Somatic Antigens in *Salmonella* by Phage Infection leading to Lysis or Lysogeny.** *Virology.* New York. 1958, Feb., v. 5, No. 1, 68–91, 4 figs. [30 refs.]

"The conversion of *Salmonella anatum* (group E_1, somatic antigens 3, 10) to group E_2 (antigens 3, 15) by infection with phage ϵ^{15} and its virulent mutant ϵ^{15} *vir* has been analyzed. Antigen 15 appears in the cells within a few minutes after infection with either phage. The receptors for another phage, ϵ^{34}, which can be adsorbed only by cells with antigen 15, appear with the new antigen. The receptors for phage C_{341}, which is adsorbed only by cells with antigen 10, disappear following infection. In the early stages the cells have both antigens 10 and 15 and both sets of phage receptors. The cells that survive infection segregate lysogenic and nonlysogenic cells in their progeny. In the nonlysogenic segregants the changes in antigenic structure and in phage receptors initiated by phage infection persist for several generations; later, the cells revert to the typical E_1 condition. The results indicate that the converted characters are controlled by vegetative phage as well as by prophage. Their bearing on the mechanism of conversion is discussed."

Beumer-Jochmans, M. P., Dirkx, J. & Oleffe-Koopmanisch, S. Effet du calcium sur la pénétration d'un phage dans certaines bactéries sensibles. [**Effect of Calcium on Phage Penetration into certain Sensitive Bacteria**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 771–80. [11 refs.]

Phage H-SHPB (Ca) adsorbs to *Shigella flexneri* F6S in the absence of Ca ++, although phage multiplication does not occur [this *Bulletin*, 1956, v. 31, 1253]. When Ca ++ were added to the culture, phage multiplication immediately began. In the absence of Ca ++, the adsorbed phage could be neutralized specifically by phage antiserum, or detached from the host cell by the action of a Waring blendor. In the presence of Ca ++, phage antiserum or mixing in a Waring blendor did not reduce the number of infective centres. The action of Ca ++ was specific, and no other ions, monovalent or divalent, prevented all the adsorbed phage from being neutralized by antiserum. The phenomenon depended upon the S character of the bacteria: once phage had adsorbed to *Sh. flexneri* strains F6R or Y6R, it was never neutralized by antiserum whether or not Ca ++ were present.

It appears, therefore, that in the absence of Ca ++ adsorption occurs normally but injection of DNA by the phage H-SHPB (Ca) into the bacterium is inhibited by the S character of the cell. The specificity of Ca ++ in reversing this inhibition would suggest that an enzyme reaction is involved in overcoming the barrier before DNA injection and phage multiplication can proceed.

Janice Taverne

Mercer, E. H. **An Electron Microscopic Study of Thin Sections of Bacteria and Bacteriophage Grown on Agar Plates.** *Biochem. et Biophys. Acta.* 1959, July, v. 34, No. 1, 84–9, 9 figs. [13 refs.]

"A method of preparing thin sections of bacteria and bacteriophage growing on conventional agar plates is described. Fixation using buffered osmium tetroxide solutions or permanganate must be followed by an immediate post-fixation in uranyl acetate solutions, which appear to stabilise the nucleic acid in the form of thin filaments ($\backsim$50 Å).

"The course of infection of *E. coli* by T2 phage is described. The phage appears to attach to the membrane of the bacterium by means of a small double layered disc at the end of the tail plug of the tubular tail sheath. Various aggregates within infected bacteria may represent stages in phage development. The nuclear core forms first and the head membrane later. Free tails have also been noted.

"On lysis the cell membranes form large numbers of small vesicles to which phage also attach."

FLAKS, J. G., LICHTENSTEIN, Janet & COHEN, S. S. **Virus-Induced Acquisition of Metabolic Function. II. Studies on the Origin of the Deoxycytidylate Hydroxymethylase of Bacteriophage-Infected** *E. coli*. *J. Biol. Chem.* 1959, June, v. 234, No. 6, 1507–11, 4 figs. [32 refs.]

BHASKARAN, K. **Observations of the Nature of Genetic Recombination in** *Vibrio cholerae*. *Indian J. Med. Res.* 1959, May, v. 47, No. 3, 253–60. [11 refs.]

Although strains of *Vibrio cholerae* which were lysogenic for phage 129 formed plaques on indicator strains, no free phage could be detected in the culture. When the bacteria were removed by filtration or killed with toluene, all the phage was also lost. No plaques were produced when a streptomycin-sensitive lysogenic vibrio was grown in the presence of streptomycin and plated on a streptomycin-resistant indicator strain. Thus it appeared that phage 129 was very closely associated with the vibrio, never being liberated into the medium, and that infection giving rise to plaques was necessarily mediated by contact between the lysogenic cell and the indicator strain.

Recombination experiments were done with auxotrophic vibrios, and prototrophic recombinants were selected. It was found that recombination did not occur unless one of the parents was lysogenic with phage 129. Unselected markers in the recombinants, *e.g.* motility or antigenic type, were found to correspond to those from one or other parent in the cross. Some recombinant prototrophs appeared to be unstable and auxotrophs of one parental type segregated from the prototrophs, indicating that a diploid state might persist. Some recombinants were of dual antigenic type (Hikojima) suggesting that the genetic determinants of the antigenic types Ogawa and Inaba were allelic in the parents.

The author puts forward the hypothesis that phage 129, in this strain of vibrio, acts as a fertility factor. He symbolizes lysogenic strains as P + and non-lysogenic as P −, on analogy with the fertility factor F of *Escherichia coli*. Mating did not occur between P − strains. Recombinants were only obtained when one or both of the parents were P +, but there was no evidence of a polarity between P + and P − strains, *i.e.* that one acted as a receptor and the other a donor, as in the *E. coli* system. (Phage-mediated transduction is not considered to be a likely explanation because of the absence of free phage and the inseparable association of phage and viable vibrios.)

[This is certainly an interesting hypothesis, but as presented here does not appear to be based on very strong evidence.] *Janice Taverne*

ZIERDT, C. H. **Preservation of Staphylococcal Bacteriophage by means of Lyophilization.** *Amer. Clin. Path.* 1959, Apr., v. 31, No. 4, 326–31, 2 figs. [10 refs.]

The author describes a method for preparation and lyophilization of the routine staphylococcal typing phages. Preparation is by short incubation of host-cell system on trypticase soy agar plates containing 0·1% $CaCl_2$. After overnight refrigeration the lysates are harvested by pipette after addition of 0·5–1·5 ml. of broth.

Titres of 2 lysates prepared in this way were 1/100,000, others were 1/10,000. Unfiltered lysates were mixed with equal quantities of double strength skim milk and lyophilized in 0·2 ml. amounts. Preparations were reconstituted by the addition of 1 ml. of broth (1/10 dilution of original material). Titres of phages immediately after lyophilization were 1/10,000 (14), 1/1,000 (12), 1/100 (1). There was a slight drop in the titres of phages 6 and 44A after 1 month storage but titres of other phages tested remained the same for between 3 and 8 months.

[Most workers preparing these phages for routine typing would regard titres below 1/5,000 as too low for use and the method described as unsuitable for preparation of large quantities of material. They would also consider the removal of unlysed host bacteria by some method essential. Residual living host cells may lead to confusion of the typing pattern. All host cells used in propagating these phages are lysogenic; contaminating cells in phage preparations may grow on typing plates and release phage which may lyse the strain under test. Failure to remove living host cells may account for the drop in titre (by adsorption) of unlyophilized preparations reported by the author. Preparations containing living cells are also unsuitable for experimental work. In the reviewer's experience bacteria-free filtrates of these preparations can be stored at 4°C. for several years with no loss of titre and lyophilization of routine preparations is generally unnecessary.] *M. Patricia Jevons*

POSPELOVA, V. V. **The Biological Characteristics of Diphtheria Phages — II. Phage Adsorbability. The Properties of Secondary Phage-Resistant Variants of** *Corynebacterium diphtheriae*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1798–802. [10 refs.] [Translated from Russian.]

Experiments were done with 5 diphtheria phages, previously described [this *Bulletin*, 1959, v. 34, 684]. Their rate of adsorption to a strain of *Corynebacterium diphtheriae* type *gravis* was measured and found to resemble that of T5 and of diphtheria phage C of GROMAN and LOCKART [*ibid.*, 1954, v. 29, 99]. Bacteria resistant to each of the 5 phages were isolated; the resistant strains retained their original sugar fermenting properties and did not lose their toxigenicity. 2 of the resistant variants were resistant to all 5 phages, the other 3 displayed different sensitivities. Antisera prepared against each phage did not have very high neutralizing activity, even against the homologous phage. However, it was shown by cross-neutralization tests that these 5 independently isolated phages were all antigenically related. *Janice Taverne*

DROZHEVKINA, M. S. & KHARITONOVA, T. I. **Lysogeny in Brucella.** *Problems of Virology*. London. 1958, v. 3, No. 2, 96–100, 3 figs. [24 refs.] [Translated from Russian.]

The isolation of phages from a proportion of cultures of *Brucella melitensis*, *Br. abortus* and *Br. suis* has been

previously reported [DROZHEVKINA, this *Bulletin*, 1959, v. 34, 582]. Lysogenic phages have now been isolated from 7 out of 24 strains of *Br. melitensis*, which were apparently free of phage, by exposing the cultures to repeated irradiation by UV light; this procedure also altered the colonial form.

It is reported that one strain of *Br. melitensis* isolated from the blood of a patient unexpectedly retained its Vi antigen upon culture. It was lysed by "Vi-phages" and agglutinated by Vi antiserum but not by O antiserum. After UV-irradiation an "O-phage" was released. Later the strain lost its phage, and it was noticed that the non-lysogenic strain was then agglutinated by O, but not by Vi, antiserum.

Janice Taverne

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

v. KERÉKJÁRTÓ, B. & HIERONYMI, B. Über die Vermehrung einiger tierpathogener Virusarten in Epithelzelkulturen von Schweineniere. [**The Multiplication of Certain Viruses Pathogenic for Animals in Cultures of Pig Kidney Epithelial Cells**] *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 469–79. [16 refs.]

Cultures of cells have been obtained from the kidneys of young or adult pigs and have been carried through numerous subcultures. The cells supported the growth of herpes, pseudorabies and B viruses, which produced cytopathic effects at the first passage, but no evidence could be obtained of the multiplication of JHM, the 3 types of poliomyelitis or of 8 types of group A Coxsackie viruses. Columbia-SK virus multiplied readily in the cultures, but encephalomyocarditis virus could only be adapted with a certain amount of difficulty; the cultures also partly supported the growth of 2 strains of tick-borne encephalitis virus (Russian spring-summer and Central European encephalitis viruses).

D. J. Bauer

v. KERÉKJÁRTÓ, B. & HIERONYMI, B. Zur virologischen Verwendung von Hammelnierenzellkulturen. [**The Use of Sheep Kidney Cell Cultures in Virology**] *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 480–84, 4 figs. [12 refs.]

An investigation has been made of the possibility of using trypsinized cultures of sheep kidney cells for the cultivation of viruses. The growth period was 7–9 days, and the cultures could be maintained for 3 weeks; subcultures could readily be obtained from the primary culture. The cultures were susceptible to infection with pseudorabies, B and herpes viruses, which could be maintained through several passages with the production of characteristic cytopathic effects. Tick-borne encephalitis virus (Russian spring-summer encephalitis and 3 European strains) grew less readily. *D. J. Bauer*

BRENNER, S. & HORNE, R. W. **A Negative Staining Method for High Resolution Electron Microscopy of Viruses.** *Biochim. et Biophys. Acta.* 1959, July, v. 34, No. 1, 103–10, 6 figs. [16 refs.]

WHEELER, C. E. & CANBY, C. M. **Influence of Specific Antibody on Herpes Simplex Infections in Tissue Culture.** *Arch. Dermat.* 1959, Jan., v. 79, No. 1, 86–93, 4 figs. [22 refs.] Discussion 93–5.

In a study of the persistence of herpes infection in the presence of specific neutralizing antibody observations were made on HeLa cell cultures infected with the ST, CR or HF strains of herpes virus and nourished with medium containing either normal or human specific immune serum. In the absence of antibody the virus infection destroyed the cell sheet in 5–10 days, whereas in the presence of antibody the infection was limited to the formation of plaques which enlarged to become confluent, after which they were replaced by a new growth of apparently uninfected cells. The cultures could be maintained in a state of chronic infection with regrowth for as long as 8 months, and this condition could be maintained for at least 16 subcultures of cells in the presence of antibody. No tendency to the development of a latent or inapparent infection could be observed. *D. J. Bauer*

DUMBELL, K. R. & NIZAMUDDIN, M. **An Agar-Ge Precipitation Test for the Laboratory Diagnosis of Smallpox.** *Lancet.* 1959, May 2, 916–17, 1 fig.

The authors describe a gel precipitation technique which appears to give rapid and specific identification of variola and vaccinia virus antigens. Within 4 or 5 hours of setting the test up it is possible to determine whether scabs or vesicle fluid from a suspected case of smallpox contain variolous antigen or not. The test is easily prepared: the suspected material is put up against 2 dilutions of a hyperimmune-rabbit antivaccinial serum and a known positive antigen is included as a control. A further check is provided by a reservoir containing normal rabbit serum. [This method should undoubtedly play an important part in the laboratory diagnosis of smallpox, especially since its efficiency is not impaired by sterilizing the suspected antigen with 0·2% formalin.] *Colin Kaplan*

FAUCONNIER, B. Utilisation des hématies hyperformolées en virologie. II.—Mise au point d'un complexe virus-hématies de longue conservation, utilisable pour le diagnostic des oreillons par une méthode d'inhibition de l'hémagglutination simplifiée. [**Use of Hyperformolized Erythrocytes in Virology. Preparation of a Virus-Erythrocytes Complex which can be preserved for a Long Time and used for the Diagnosis of Mumps, by means of a Simplified Haemagglutination-Inhibition Test**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 110–13.

The stability of mumps virus haemagglutinins and of

red cells treated by hyperformolization [this *Bulletin*, 1949, v. 24, 371; 1957, v. 32, 10, 382] have made it possible to prepare a virus-red-cell mixture for use in inhibition tests which will remain fit for use during storage for at least 2 months at 4°C. Chick red cells were treated with formalin and gassed with carbon monoxide, and both procedures were then repeated; the red cells were then stored at 4°C. The virus-red-cell mixture was prepared by mixing 2 cc. of treated red cells with 10 cc. of allantoic fluid containing mumps virus and 8 cc. of buffered saline or glycerol. Before use the mixture was diluted 1 : 20 with buffered saline; it was then mixed with equal volumes of 2-fold dilutions of antiserum and the inhibition titre was read after exposure to room temperature for 2 hours.

D. J. Bauer

NASTAC, E. **The Effect of Mumps Virus on the Spontaneous Rat Sarcoma.** *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 105–8.

" 1. Mumps virus from allantoic fluid of infected chick embryos had a lytic activity on spontaneous rat sarcoma, if the rats bearing the tumour were inoculated intravenously.

" 2. Clinically the oncolytic activity of mumps virus was manifested either by complete resorption of the developing cancer tissue (in 36.4%), or by necrosis, cicatrization and loss of cancer tissue, observed in many cases, or by suspension of growth of the tumour, the size of tumours in inoculated animals being considerably smaller than that in the controls.

" 3. Microscopic examination of sections of the tumours following mumps virus administration revealed disseminated microabscesses containing degenerate tumour cells in the tumour parenchyma associated with numerous granulocytes and arrest of mitosis in giant cells.

" 4. The virus had no influence on the ability of the tumour to be transplanted in the first passage."

HINZ, R. W. & SYVERTON, J. T. **Mammalian Cell Cultures for Study of Influenza Virus. I. Preparation of Monolayer Cultures with Collagenase.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 19–22, 7 figs. [12 refs.] **II. Virus Propagation.** *Ibid.*, 22–6, 3 figs.

I. A method is described for the preparation of primary monolayer cultures of human, rabbit and pig lung tissues. Cell suspensions were obtained by treating the tissues with a 0·01% concentration of collagenase in phosphate-free salt solution. The advantage of collagenase over trypsin for the preparation of lung tissue suspensions is discussed.

II. The capacity of human, rabbit and pig lung and pig kidney tissue cultures to support the multiplication of influenza viruses was investigated. Cultures were prepared with cell suspensions obtained by treatment of tissues with collagenase. Human lung cultures supported the multiplication of influenza A (Asian and PR8) and B (Lee) viruses but not of a swine strain. Multiplication of human strains in human lung cultures was accompanied by minimal cytopathic effects. Pig lung cultures supported the multiplication of both human and swine influenza viruses but showed greater susceptibility to the latter as shown by the more marked cytopathic effects and higher infectivity titres reached. Propagation of swine influenza virus in pig kidney cultures could be demonstrated in the absence of cytopathic effect. Rabbit lung cultures did not support the multiplication of human or swine influenza viruses.

H. G. Pereira

PAUCKER, K.; BIRCH-ANDERSON, A.; VON MAGNUS, P. **Studies on the Structure of Influenza Virus. I. Components of Infectious and Incomplete Particles** [PAUCKER, BIRCH-ANDERSON & VON MAGNUS]. *Virology.* New York. 1959, May, v. 8, No. 1, 1–20, 4 figs. [36 refs.] **II. Ultrathin Sections of Infectious and Non-infectious Particles** [BIRCH-ANDERSON & PAUCKER]. *Ibid.*, 21–40, 13 figs. [36 refs.]

1. Elementary bodies, haemagglutinin and soluble antigen (also referred to as G antigen by German workers) obtained from standard and incomplete PR8 influenza virus were studied by electron microscopy, analytical centrifugation and electrophoresis. Purified virus preparations were submitted to ether treatment and fractionated by differential centrifugation. Sedimentation constant and electrophoretic mobilities of elementary bodies, haemagglutinin and soluble antigen present in complete and incomplete virus preparations are presented. Haemagglutinin from standard virus preparations was associated mainly with spherical bodies ranging in diameter from 35 to 40 mμ and to lesser extent with ghost-like structures. In incomplete virus preparations most of the haemagglutinating activity was associated with ghosts. The 2 haemagglutinating components could be distinguished by their reactivity with guineapig and chicken erythrocytes. The soluble antigen obtained from purified virus preparations was correlated with rod-like structures measuring about 17 mμ in diameter and ranging in length from 55 to 140 mμ. These structures were obtained in great numbers from standard virus materials but demonstration of its presence in incomplete virus preparations could only be achieved after extensive concentration.

II. The morphology of complete and incomplete forms of influenza virus (strain PR8) was studied by electron microscopy of sprayed virus suspensions and of ultrathin sections of virus pellets. Incomplete virus was obtained by undiluted passages of fully infective or partially inactivated virus in fertile eggs and by HeLa cell passages. Heat-inactivated virus and cell-associated non-infectious virus present in chorio-allantoic membranes supporting the multiplication of standard virus were also examined. Correlations between morphology, infectivity, haemagglutinating and complement-fixing activities of the different virus preparations were investigated.

Ultra-thin sections of fully infectious virus were shown to contain uniform particles with a diameter of about 70 mμ with an electron-dense inner region measuring 45 mμ in diameter, limited by a membrane 4 mμ thick which is in turn surrounded by a zone of lower density about 10 mμ wide and a less clearly defined outer membrane. Incomplete virus preparations

obtained by undiluted serial passages or by the use of partially inactivated inocular contained particles rather irregular in shape and size and lacking the electron-dense centres. Non-infectious virus derived from HeLa cells or from egg membranes producing standard virus also lacked the dense centres and consisted mainly of ghost-like structures and aggregates of small flattened bodies. Heat-inactivated standard virus contained well-defined electron-dense centres and showed surface changes presumably due to protein denaturation.

The significance of morphological differences observed among the various preparations of non-infectious virus is discussed. *H. G. Pereira*

Reinhard, K. R. & McGraw, J. C. **Simple Means of obtaining Concentration of Influenza Haemagglutinating Antigen.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 557–8.

Allantoic fluids from fertile eggs infected with influenza viruses showed a flocculent precipitate appearing within a few days of storage at 4° to 6°C. Most of the haemagglutinating activity of the original fluids was found to be associated with this precipitate. Concentrated preparations of influenza A and B haemagglutinins obtained by this procedure were stable on storage at 4° to 6°C. and suitable for use in haemagglutination-inhibition tests. *H. G. Pereira*

Drescher, J. & Lange, F. C. Über Hämagglutinin- und Antikörpergehalts-bestimmungen. IV. Mitteilung: Beschreibung eines photometrischen Verfahrens zur Bestimmung von spezifisch und von unspezifisch die Hämagglutination hemmenden Antikörpern. **[The Determination of Haemagglutinin and Antibody. IV. Description of a Photometric Procedure for the Determination of Specific and Unspecific Inhibiting Antibodies]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 185–95, 4 figs.

A previously developed photometric method for the titration of influenza virus [this *Bulletin*, 1958, v. 33, 406 *bis*] has been adapted to the titration of inhibiting antibody and unspecific inhibitors. By means of the method, which is based on the applicability of the Freundlich isotherm to the interaction between influenza virus and antibody, the concentration of antibody present in a particular dilution of serum can be determined. When the product of the dilution and the concentration of antibody in the same dilution were plotted against dilution the expected straight line parallel to the abscissa was only obtained in the higher dilutions. The deviation of the initial part of the line, in which measured antibody content had a negative regression on dilution, was reduced by treatment of the serum with a filtrate of *Vibrio cholerae* and abolished by treatment with trypsin, and was therefore due to the interaction of virus with unspecific inhibitor. The 2 parts of the curve therefore give a measure of the content of specific inhibiting antibody and unspecific inhibitor without the necessity of treating the serum with trypsin or *V. cholerae* filtrate. In the presence of antibody to other strains of virus (unspecific inhibiting antibody) a straight line parallel to the abscissa could not be obtained, and this finding could be used as a test of specificity. *D. J. Bauer*

Seto, J. T., Hickey, Betty J. & Rasmussen, A. F., Jr. **Some Biological Characteristics of Asian Influenza Isolates.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 672–6, 1 fig. [11 refs.]

Biological properties of 5 strains of Asian influenza virus were studied and compared with those of other influenza A viruses (PR8 and FM1). Haemagglutination titres in allantoic fluids of eggs inoculated with Asian strains were consistently lower than those obtained with PR8 or FM1. Toxigenic properties were determined by cytotoxicity in tissue cultures (HeLa and human amnion cells), by neurotoxicity for mice and by xanthine oxidase inducing activity in mouse lung homogenates and revealed no significant differences between Asian, PR8 and FM1 strains. Asian strains did show, however, a higher neuraminidase activity to urine mucoprotein than PR8 and FM1.

H. G. Pereira

Polley, J. R. **Variables influencing the Preparation of Influenza Vaccines with Formaldehyde.** *Canadian J. Microbiol.* Ottawa. 1959, Apr., v. 5, No. 2, 237–44, 2 figs.

The effect of *p*H and temperature on the inactivation of influenza virus infectivity and haemagglutinating property was investigated. Inactivation rates increased with increasing *p*H and this effect was more marked at 4°C. than at 37°C. The conditions required to ensure virus inactivation with little loss of haemagglutinin titres are defined and vaccines obtained by different methods were tested in animals for antigenicity and for protection against virus challenge. A correlation was found between haemagglutinin titres and immunizing properties of the vaccines. Lyophilized vaccines stored for 2½ years were shown to retain haemagglutinating and immunizing activities.

H G. Pereira

Andrewes, C. H., Bang, F. B., Chanock, R. M. & Zhdanov, V. M. **Para-Influenza Viruses 1, 2, and 3: Suggested Names for Recently Described Myxoviruses.** [Correspondence.] *Virology.* New York. 1959, May, v. 8, No. 1, 129–30.

The name Para-influenza is proposed for a group of Myxoviruses having certain common properties which allow their distinction from influenza virus types A, B and C. Para-influenza viruses are divided into the following sub-groups:

(1) *Myxovirus para-influenzae 1* (para-influenza 1) including the Sendai virus (= haemagglutinating virus of Japan = influenza D) and haemadsorption virus 2.

(2) *Myxovirus para-influenzae 2* (para-influenza 2) represented by the croup-associated (CA) or laryngo-tracheo-bronchitis virus.

(3) *Myxovirus para-influenzae 3* (para-influenza 3) represented by the haemadsorption virus 1.

Para-influenza viruses have some properties in common with mumps and Newcastle disease viruses but a change of name of the latter agents is considered unwise at the moment.

The names proposed have been approved by the Virus Subcommittee of the International Nomenclature Committee. *H. G. Pereira*

PERKINS, F. T. & EVANS, D. G. **British Standard Poliomyelitis Antisera Types 1, 2, and 3.** *Brit. Med. J.* 1959, June 20, 1549–53, 1 chart.

High-titre poliovirus neutralizing sera were prepared against the 3 types of poliovirus (Type 1, Mahoney; Type 2, M.E.F.1; Type 3, Saukett). Each monospecific serum was diluted to give a neutralizing antibody titre between 1/500 and 1/1,000 in 6% dextran and freeze-dried in 1 ml. amounts in ampoules. This paper describes tests performed on these sera before their adoption as British Standard poliomyelitis antisera. Each ampoule contained 10 units of specific antibody, thus enabling the comparison of unknown sera in terms of units instead of titres. The ampoules proved consistent both in weight and in titre. Reconstituted sera were stable at 4°C. for 5 months. The dry sera were very resistant to heat.

A collaborative experiment to assess the value of these sera was undertaken by 4 laboratories using the same technique of serum titration by inhibition of the cytopathic effect of poliovirus on monkey kidney cells, and by 1 laboratory using a modification of the colour test described by SALK, YOUNGNER and WARD [this *Bulletin*, 1955, v. 30, 184]. Each laboratory performed 4 replicate titrations of the 3 standard sera and 18 (6 of each type) unknown sera. The results were very consistent. All the laboratories obtained replicate results within 2-fold and for all but 2 out of the 18 unknown sera the difference between laboratories was within 4-fold, when the results were compared in terms of units (by dividing the mean titre of the serum under test by that of the standard and multiplying by 10). 2 of the sera for each type were obtained by making a 5- and 25-fold dilution of one of the sera under test. The various laboratories obtained ratios between these sera very close to the theoretical figure. These sera should prove of great value in standardizing the results of poliovirus neutralizing antibody titration. They can be obtained from the Department of Biological Standards, National Institute for Medical Research, Mill Hill, London. *A. J. Beale*

PAPAPANAGIOTOU, J. [**Isolation of Polioviruses Type I, II, and III from Stool Specimens from Greece, 1958.**] *Acta Microbiologica Hellenica.* Athens. 1959, Jan.–Apr., v. 4, Nos. 1/2, 24–8. [In Greek.]

The English summary appended to the paper is as follows:—

"In a previous communication (Acta Microbiologica Hellenica, 1958, 3, 249) the isolation of 9 strains of poliovirus Type I from stool specimens collected in September 1958 was reported.

"In November and December 1958, one stool specimen was collected from each of 21 patients with a clinical diagnosis of paralytic poliomyelitis. All the patients were treated in the Hospital for Infectious Diseases, Athens. The stool samples were stored at 20°C in the department of Bacteriology of the University of Athens. The specimens were shipped to Statens Seruminstitut, Copenhagen, by air without refrigeration.

Methods: "Virus isolations as well as titrations and typing of the isolated strains were carried out in roller tube cultures of trypsinized monkey kidney cells by the methods currently used for diagnostic work in the Polio Department of the Institute.

Results: "From the 21 stool specimens, fourteen strains of poliovirus Type I, one strain of poliovirus Type II, and one strain of poliovirus Type III were isolated (see table). Including the previously isolated 9 strains of poliovirus Type I, the isolated strains of poliovirus from Greece in 1958 thus represent 23 strains of Type I, one Type II and one Type III.

"The polio epidemic in Greece in 1958 was thus probably due to poliovirus Type I, although the other 2 types were also found to be present.

"The desirability of virological and serological studies in every case of clinical poliomyelitis is discussed."

EKLUND, C. M., HADLOW, W. J., PICKENS, E. G. & GERLOFF, R. K. **Detecting Poliovirus in Vaccine Lots used in Idaho in 1955.** *Pub. Health Rep.* Wash. 1959, Jan., v. 74, No. 1, 60–66.

2 batches of poliovaccine (Nos. 6058 and 6039) were inoculated into 32,000 children aged 6–8 in Idaho in 1955. Approximately one-half the children lacked Type 1 antibodies and 17 succumbed with paralytic poliomyelitis. This paper describes tests on these batches in monkeys, from which it is estimated that monkeys in which the test is properly performed are very much more sensitive than children in detecting poliovirus (about 500 times more sensitive), since about 40% of the monkeys inoculated yielded a poliovirus. The most sensitive route of inoculation was intraspinal. This was performed using a special 1¼-inch 25-gauge needle with a hole in the side of the shaft ⅛-inch from the occluded end of the needle. This was inserted into 1 of the first 3 lumbar interspaces and the inoculum (0·6 ml.) directed in the long axis of the cord. If the inoculation was in the correct site there was a contraction of 1 leg on insertion of the needle followed as the inoculation was made by a seizure involving both legs and the back muscles. Severe paralysis usually followed the injection but this did not interfere with a diagnosis of progressive poliomyelitis. All the monkeys received cortisone. Virus isolations have to be attempted from the CNS, blood, lymphoid tissue and brown fat for the best results. Virus was more readily detected in preparations treated with merthiolate (with or without versene). This was probably due to the action of merthiolate on Type 2 antibody formation. Thus Type 1 or 3 antibodies were rarely detected, but Type 2 antibodies were usually present after the use of untreated vaccine. Merthiolate treatment resulted in no Type 2 antibody response and even in the presence of versene the Type 2 antibody response was much inferior to that after untreated vaccine.

All 3 types of poliovirus were isolated from these 2 lots of vaccine although all the cases were due to Type 1 virus. On 4 occasions 2 types of virus were obtained from a single monkey. Rhesus, African green and cynomolgus monkeys were used in this investigation. Type 2 only was recovered from African green monkeys, but otherwise the sensitivity of the different types of monkey were similar. It is reassuring that the monkey safety test can be so much more sensitive to residual poliovirus than children. *A. J. Beale*

PRIGGE, R., GÜNTHER, O. & BONIN, O. Untersuchungen zur Wirksamkeitsprüfung von Poliomyelitis-Impfstoffen. [**Investigations on the Potency Testing of Poliomyelitis Vaccines**] *Ztschr. f. Immunitatsf. u. Exper. Therap.* 1959, Jan., v. 117, No. 1, 22–44, 3 figs. [18 refs.]

Sources of error in the determination of the immunizing power of poliomyelitis vaccines are discussed in detail, with particular reference to the determination of relative potency from a comparison of the antibody content of antisera produced by test vaccines in comparison with a previous result from a standard antiserum obtained with a standard vaccine. It would be desirable to carry out control immunization with a standard vaccine in parallel with each investigation of test vaccines, but this is not possible in view of the fact that a stable dried vaccine for reference purposes cannot be prepared, and the method of testing can therefore only be regarded as qualitative. A description is given of the German minimum requirements for poliomyelitis vaccines, which are based on the production of antibody in guineapigs, and the results of the comparative testing of 9 German and foreign commercial vaccines according to the German requirements are presented in tables.
D. J. Bauer

PAUL, S., GUPTA, N. P. & GUPTA, S. P. **Enteric Viruses from Sporadic Cases of Aseptic Meningitis/Encephalitis.** *J. Indian Med. Ass.* 1959, Apr. 16, v. 32, No. 8, 312–6. [20 refs.]

27 patients with a diagnosis of meningitis or encephalitis, admitted sporadically to the children's hospital in Lucknow, were investigated by the inoculation of stool suspensions and sometimes cerebrospinal fluids into monkey kidney tissue culture. Also stools from 8 healthy children and 7 patients with other febrile illness were examined.

14 agents were isolated of which 8 were identified thus: poliovirus type 1, 3; type 2, 1; type 3, 2; Coxsackie B5, 2. The remaining 6 viruses could not be identified, 2 produced Coxsackie B type lesions in suckling mice. All but 2 agents (both untyped) were neutralized by U.S. gamma globulin but none by pooled monkey serum. 4 strains of virus were isolated from healthy children and 2 were polioviruses. Coxsackie B5 was isolated from the cerebrospinal fluid of a patient with meningitis who also excreted type 2 poliovirus in the stools. 2 of the patients yielding poliovirus type 1 were paralysed and the patients yielding type 3 poliovirus and Coxsackie B5 virus had aseptic meningitis. The elucidation relationship between the other viruses and the disease of the children awaits their indentification and the determination of the antibody responses of the patients. *A. J. Beale*

HAMMON, W. McD., YOHN, D. S. & PAVIA, Rose A. **ECHO Virus Type 12, Isolation and Characteristics.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 743–5. [10 refs.]

This paper describes the characteristics of the prototype ECHO virus type 12 (Travis strain). An antiserum prepared against this strain by Dr. A. WENNER was found capable of neutralizing in addition to ECHO 12, types 1, 8 and the original prototype ECHO 13, although ECHO 12 virus was not neutralized by antisera to ECHO 1, 8 or 13. The original ECHO 13 prototype has been found to contain ECHO 1 virus as a contaminant and the new prototype is not neutralized by ECHO 12 antiserum [HAMMON *et al.*, this *Bulletin*, 1959, v. 34, 837]. Antiserum made from a pool of ECHO 12 virus purified by terminal dilution failed to show any cross-reactions with similarly purified ECHO types 1, 8 or 13 while neutralizing ECHO 12 to high titre. The purified ECHO 12 prototype virus was not pathogenic for suckling mice or 7-day-old chick embryos. Similarly no disease was caused in guineapigs, rabbits or rhesus monkeys after either intracerebral or intramuscular inoculation. Besides growing in monkey kidney cells the virus grew well in HEP 2, HeLa and Detroit 504 Fb-L cell lines and in human amnion cells. On the other hand it did not grow in a monkey heart cell line or in primary cultures of hamster or gerbil cells. The virus produced large plaques (10–14 mm. in diameter) on monkey kidney cells and tiny plaques on patas monkey kidney cells. The virus does not agglutinate chick red cells but does agglutinate human group O at 4, 25 or 37°C. Infected tissue culture fluids produce infectious virus, haemagglutinin and complement-fixing antigens.

Besides the first isolations from the Philippines made in Hammon's laboratory the virus has also been isolated in other parts of the United States and in Mexico. About half the sera from 30 Americans at Clark Air Force Base on the Philippines contained antibodies to ECHO 12 virus and antibodies were also present in a sample of Japanese gamma globulin. ECHO 12 virus falls into HSIUNG and MELNICK's (*Ann. N.Y. Acad. Sci.*, 1958, v. 70, 342) ECHO virus group B, which also contains types 7 and 8. Their classification is as follows:—

Group A (*patas* negative)

1. Small irregular plaques with hazy centres, on rhesus only: ECHO 3 (Berardi strain), 4, 6′, 6″, 9, 11, 14, 15, 16, 17, 18, 19.
2. Small irregular plaques with clear centres, on rhesus (occasionally tiny delayed plaques on *patas*): ECHO 1, 13.
3. No plaques on either rhesus or *patas*: ECHO 2, 3, 5, 6, 10.

Group B (*patas* positive)

1. Large circular plaques on rhesus and *patas*: ECHO 7.
2. Small or medium-sized plaques on rhesus and tiny delayed plaques on *patas*: ECHO 8.
3. Large circular plaques on rhesus and tiny delayed plaques on *patas*: ECHO 12. *A. J. Beale*

WINN, J. F. & BENNINGTON, E. E. **An Attempt to recover WEE from Nasal Mites of Sparrows.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 135–6.

"1. Twenty days after 44 English sparrows were each inoculated with 140 chick LD_{50} amount of WEE virus, the collected mites were devoid of virus using Chamberlain's 'wet', chick method of isolation. 2. Nasal mites of the English sparrow are probably not important as reservoirs of Western encephalitis virus."

TRAUB, E. Über die Immunität der weissen Maus gegenüber dem EEE-Virus. I. Mitteilung: Wirkung von Immunserum *in vivo*. [**Immunity of White Mice to Equine Encephalomyelitis Virus. I. Effect of Immune Serum** *in vivo*] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Jan., v. 117, No. 1, 70–94. [17 refs.]

Mice were infected subcutaneously with eastern equine encephalomyelitis virus and 1–96 hours after infection hyperimmune serum obtained from mice immunized with infected mouse-brain material was injected intravenously. The mean incubation period in mice given antiserum up to 24 hours after infection was 18–41 days, compared with 5–7 days when the antiserum was given after 48–96 hours. Immune serum from mice immunized with chick embryo virus, or from chickens, was much less effective in conferring passive immunity. Mouse hyperimmune serum still exerted a therapeutic effect when given after 120 hours, when the virus had already reached the brain. In treated mice developing symptoms after a prolonged incubation period the neutralizing antibody titre of the serum was very low, and the virus had evidently persisted in the central nervous system without evoking active immunity. It was further shown that passive immunization hindered the development of active immunity. *D. J. Bauer*

LAVILLAUREIX, J. & REEB, E. Culture *in vitro* du virus West Nile. [**Culture of West Nile Virus** *in vitro*] *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 941–8, 2 figs. on pl. & 1 graph.

The virus used had undergone 38 intracerebral mouse passages. 3 continuous human-cell lines were used: HeLa, KB and Detroit-6. Foetal human, guineapig, mouse, gerbil and pig kidney cells were also used. The virus multiplied in all the cells tried. Cytopathogenic effects were seen in the first passage in Detroit-6 cells but was irregular in the first few passages in HeLa and KB cells. With lower virus doses plaque formation was observed. 18 serial passages were carried out in KB and Detroit-6 cells and the virus was re-identified at the end. After a short eclipse phase the virus reached its maximum titre of about 10^{-8} in 24 hours after infection.

In HeLa and KB cells passage greatly diminished the pathogenicity of the virus for mice: before adaptation to tissue culture 10^6 ID50 of virus killed mice in 4–6 days but at the 7th passage $10^{7 \cdot 25}$ ID50 caused no symptoms in the mice. This attenuated virus caused the formation of antibodies in mice and rabbits. In Detroit-6 cells and in kidney cells the pathogenicity for mice was unchanged. *C. E. Gordon Smith*

SPENCE, L. P. & THOMAS, L. **Application of Haemagglutination and Complement-Fixation Techniques to the Identification and Serological Classification of Arthropod-Borne Viruses. Studies on Chikungunya and Makonde Viruses.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, May. v. 53, No. 3, 248–55, 3 figs.

2 viruses, Chikungunya and Makonde, were isolated during the outbreak of dengue-like disease which occurred at Newala in Tanganyika in 1952–3 [*Trop. Dis. Bull.*, 1956, v. 53, 1334]. Haemagglutinins were prepared from suckling mouse brains for each virus. Chikungunya gave its highest titre at *p*H 6·4 and 37°C.; that of Makonde was at *p*H 6·8 and 22°C. or 4°C. These antigens were tested against a range of antisera to group A and B arborviruses: Chikungunya was clearly related to the group A viruses and Makonde to the group B viruses. The 2 antigens were then tested against hyperimmune mouse sera in a complement-fixation test: Chikungunya was found to be related to Mayaro virus and slightly to Semliki Forest virus; Makonde was more closely related to Uganda S virus than to any other. Cross-neutralization tests with monkey sera confirmed that Makonde is a strain of Uganda S.

Cross haemagglutinin-inhibition tests with hyperimmune sera against Chikungunya, Mayaro and Semliki viruses showed that Chikungunya was distinct but more closely related to Mayaro than to Semliki virus. Mayaro virus on the other hand appeared to be closer to Semliki than to Chikungunya virus. With sera from mice which had had only a single dose of virus Chikungunya and Mayaro viruses could easily be differentiated.

Complement-fixation tests revealed only a slight reaction between Chikungunya antigen and Mayaro serum and none between Mayaro antigen and Chikungunya serum. When the mice whose serum was used in this test were given another dose of virus their sera cross-reacted with both Mayaro and Semliki viruses but in much lower titre than in homologous tests.

Neutralization tests with intracerebral inoculation of virus-serum mixtures revealed a relationship between Chikungunya and Mayaro viruses and to a slight degree with Semliki virus. When the intraperitoneal route was used, however, strong relationships were established between Chikungunya and all the group A arborviruses used (Mayaro, Semliki, western, eastern and Venezuelan equine encephalomyelitis viruses) except Sindbis virus where there was a low degree of cross-reaction only.

2 pairs of sera from patients in the Newala outbreak showed significant rises in antibody titre against Chikungunya but not Makonde virus. The percentage of sera

with antibody to Chikungunya virus in the Newala population increased from 17 to 71 during the outbreak while that of antibody to Makonde virus fell from 43 to 32. *C. E. Gordon Smith*

ANDERSON, S. G. & ADA, G. L. **Some Aspects of the Reaction between Crude Murray Valley Encephalitis (MVE) Virus and Deoxycholate.** [Correspondence.] *Virology.* New York. 1959, June, v. 8, No. 2, 270–71.

VERGE, J., PARAF, A. & ASSO, J. Le phénomène d'adaptation spécifique des ultravirus en fonction de l'age des animaux. [**The Phenomenon of Specific Adaptation of Viruses in relation to the Age of the Animals**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 16–31, 8 figs. [23 refs.]

Neonatal rabbits infected intraperitoneally with type C foot-and-mouth disease virus developed flaccid paralysis and died after 24–48 hours; in rabbits aged 30–40 days the incubation period was prolonged to 36–48 hours and death occurred after 4–5 days with marked degeneration of the skeletal muscles and myocardium. Between the 50th and 87th passages in rabbits aged 7–35 days the titre of virus in the brain and liver fell from 10^6 to 10^4, whereas the titre in the skeletal muscles and heart rose to 10^9 LD50 per gramme. The latter change did not occur when rabbits aged 5 days were used for passage, and was therefore ascribed to physiological factors in the host and not to mutation of the virus with selection of a myotropic variant.

D. J. Bauer

JONES, B. R., COLLIER, L. H. & SMITH, C. H. **Isolation of Virus from Inclusion Blennorrhoea.** *Lancet.* 1959, May 2, 902–5, 5 figs. [21 refs.]

This paper reports the isolation of 2 strains of virus, one from a woman with inclusion cervicitis and the other from a baby with inclusion blennorrhoea, both of which were obtained by inoculating embryonate eggs by the yolk sac route. They were similar in size, appearance and staining reactions to the virus of trachoma or other members of the psittacosis-lymphogranuloma group and they possessed the complement-fixing antigen common to that group. Inclusion conjunctivitis was produced in 4 young baboons by firmly rubbing the tarsal conjunctiva with a yolk sac suspension made from the 8th egg passage of one of these strains.

S. P. Bedson

HOTTA, S. **Propagation of Dengue Virus in Tissue Culture.** *Acta Tropica.* Basle. 1959, v. 16, No. 2, 108–50, 17 figs. [Numerous refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1123.]

IMMUNITY

NEIPP, L., KUNZ, W. & MEIER, R. Selektive Erhöhung der "natürlichen" Resistenz gegenüber bakterieller Infektion durch Polysaccharide und andere Pharmaka. [**Selective Enhancement of "Natural" Resistance to Bacterial Infections by Polysaccharides and other Preparations**] *Schweiz. med. Woch.* 1959, May 16, v. 89, No. 20. 532–6. [22 refs.]

The authors first review some of the recent literature on the production of increased resistance to bacterial infection by injection of materials antigenically unrelated to the infecting organism. They then describe an extensive investigation in which 1,500 substances were tested for capacity to produce such an effect. The tests were both therapeutic and prophylactic.

In the former mice were inoculated with Type 3 pneumococcus or Type A *Klebsiella* (presumably *Klebsiella pneumoniae*) and divided into 4 groups: (1) given a sub-curative dose of sulphonamide (unspecified) orally, (2) given the substance to be tested by subcutaneous injection, (3) given both and (4) given neither. In prophylactic tests mice were given 1 dose of the substance by intravenous or intraperitoneal injection 1 or 2 days before inoculation with *Staphylococcus aureus* or *Escherichia coli*. The results with 46 substances found to possess some activity are given in one large table, which states simply the dose of the substance given in each of the 4 types of experiment (therapeutic or prophylactic, in Gram-positive or Gram-negative infection), the percentage of surviving animals, and the degree of activity ("+" "++" etc.).

The substances tested were polysaccharides from pneumococci, *Proteus* and other bacteria, from plants and from animal sources including female *Ascaris*, calf's lung and colostrum, steroid hormones, and a variety of synthetic products including salicylic acid derivatives, glucofuranosides and sphingosins. More substances were effective in therapeutic tests than in prophylactic, and more in pneumococcal infection than in others: *Proteus* polysaccharides and sphingosins showed some activity in all 4 tests.

For the somewhat bewildering details of the results the original paper should be consulted. With few exceptions (the specific immunizing activity of pneumococcus polysaccharide, the known action of steroid hormones and the possible direct antibacterial activity of salicylic acid and its derivatives) no attempt is made to explain the mechanism of the effect. It is considered that some of these effects, more particularly those specific for a particular infection, may prove to have clinical therapeutic applications. *L. P. Garrod*

FISHMAN, M. **Antibody Formation in Tissue Culture.** [Correspondence.] *Nature.* 1959, Apr. 25, v. 183, 1200–201, 2 figs.

This paper reports the formation of antibody to T2 bacteriophage and to haemocyanin by tissue cultures of rat lymph node cells treated with these antigens *in vitro*.

If antigen alone was added to the lymph node culture, antibody was not produced. If, however, antigen was incubated for 30 minutes with a washed suspension of rat macrophages from the exudate produced by an intraperitoneal injection of broth, and subsequently freed of cells by filtration, it stimulated antibody formation by the cells of lymph node tissue cultures. Antibody appeared from the fifth to the seventh day and had increased in amount by the eleventh day.

Phage antibody was assayed by neutralization of phage infectivity for *Escherichia coli* B and haemocyanin antibody by a haemagglutination method. Antibody in tissue culture fluids was concentrated before assay by ammonium sulphate precipitation, re-solution, and dialysis. *I. B. R. Duncan*

ARDAY, Florence R., PILLEMER, L. & LEPOW, I. H. **The Properdin System and Immunity. VIII. Studies on the Purification and Properties of the Third Component of Human Complement.** *J. Immunology.* 1959, May, v. 82, No. 5, 458–66. [23 refs.]

The work reported here is concerned with the purification of C′ 3 and with the properties of the purified material in immune haemolysis and in the properdin system. It is the continuation of the authors' now well-known work on the properdin system [this *Bulletin*, 1955, v. 30 83; 1956, v. 31, 226, 598, 1277; 1957, v. 32, 517, 1207].

C′ 3 is a relatively heat-stable factor which is required for most of the activities of complement. It is preferentially inactivated by zymosan. Hitherto, the partial purification of C′ 3 has been achieved only with porcine serum.

C′ 3 may be detected by its ability to restore haemolytic activity to serum which has been treated with zymosan at 37°C. (R3 assay). It has also been defined as the factor(s) in versene (EDTA) treated serum which is (are) required for the haemolysis of sensitized sheep erythrocytes (EA) which have previously been treated with C′ 1, C′ 4 and C′ 2 ($EAC'_{1,\ 4,\ 2}$). A similar system using human complement components ($EAhuC'_{1,\ 4,\ 2}$) has been used for the estimation of human C′ 3. Properdin itself is defined as an euglobulin of normal serum which is required for the inactivation of C′ 3 by zymosan.

The authors of the present paper set themselves 3 objectives: (i) isolation of C′ 3 in as pure a state as possible, using the R3 assay as indicator of the degree of purification; (ii) evaluation of the capacity of purified C′ 3 to haemolyse $EAC'_{1,\ 4,\ 2}$; and (iii) evaluation of purified C′ 3 as a source of the third component of complement in the properdin system.

Starting with human serum fraction III–1 (COHN method 9 in *J. Amer. Chem. Soc.*, 1946, v. 68, 459) as a concentrated source of C′ 3, a 100-fold purification of this component was achieved. The final fraction E IV was heterogenous on electrophoresis but was free of C′ 1, C′ 2 and C′ 4 activity and there was no detectable properdin, plasmin or C′ 1-esterase. With fresh human serum as starting material a less highly purified fraction containing C′ 3 (A IV) was obtained by bypassing the preparation of III-1.

E IV was assayed for C′ 3 activity by the R3 assay and was found to be highly active. This fraction was only slightly active in haemolysing $EAhuC'_{1,\ 4,\ 2}$ whereas earlier fractions in the purification scheme were active in this system. E IV restored the bactericidal and virus-neutralizing activity of R3 + properdin. Properdin-zymosan complex (PZ) was unable to inactivate the C′ 3 activity of E IV or of fraction III-1, though PZ was active against C′ 3 in whole serum. PZ did not reduce the C′ 3 activity of A IV but did remove the C′ 3 activity of earlier fractions.

The authors conclude that the definition of C′ 3 on the basis of the R3 and the $EAhuC'_{1,\ 4,\ 2}$ assays are are not identical and that immune haemolysis of $EAhuC'_{1,\ 4,\ 2}$ by C′ 3 is more complex than previously appreciated. [It was a satisfying experience to read this excellent but complex paper and it should be consulted for details.] *Max Sussman*

WILDE, J. & NAUMANN, G. Immunbiologische Untersuchungen an epinephrektomierten Tieren. [**Immunological Investigations in Adrenectomized Animals**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, June, v. 117, No. 6, 405–18. [44 refs.]

The English summary appended to the paper is as follows:—

"Fifty-seven cats which were immunized with Brucella abortus Bang, and had acquired a stationary immunity, were adrenectomized in Somnifen-Thiogenal anesthesia. The level of the agglutinating and complement fixing antibodies determined after the operation did not differ from those present before the operation. The changes in the protein fractions and the significant decrease in the total protein level of the serum observed after the adrenectomy were the same in 11 cats in which only a laparotomy was performed. The protein fractions of both groups showed only quantitative but no qualitative differences. The results are discussed and compared to those published by other authors."

FURNESS, G. **Effect of Cortisone on the Macrophages of Different Species of Animal.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 461–4, 1 fig. [13 refs.]

This paper describes the effect of cortisone, administered at a level which divides laboratory animals into cortisone-sensitive and cortisone-resistant species, on the numbers of leucocytes obtained from the peritoneal washings of albino rats, mice and guineapigs, and on the morphology and phagocytic power of leucocytes from the three species in cell culture.

The author shows that when guineapigs and rats are injected intraperitoneally with 36 mgm. of cortisone acetate per kgm. daily for 6 days there is a significant reduction in the number of cells obtained from the peritoneal washings of rats but not guineapigs. He further shows that hydrocortisone succinate in cell culture medium at various concentrations produces different morphological changes in cultured leucocytes obtained from guineapigs as compared with those from rats and mice and that the guineapig leucocytes are 10 to 100 times more resistant to hydrocortisone than the rat and mouse leucocytes.

He found that hydrocortisone produced no significant reduction in the phagocytic or bactericidal power of mouse cells in culture and that there was no diminution in the same action of leucocytes obtained from cortisone-treated rats and guineapigs, and that subsequent addition of hydrocortisone to the cell culture media did not affect the result.

From his experiments the author concludes that although cortisone causes changes in leucocytes, their function is relatively unimpaired and that increased susceptibility to infection in cortisone-sensitive species is due to a reduction in the number of cells.

Frank E. Russell

NELSON, E. L. & BECKER, Joan R. **The Effect of Whole-Body X Irradiation on the Bactericidal Activity of Phagocytic Cells. I. Survival of *Pseudomonas aeruginosa* within Phagocytes from Peritoneal Exudates of Mice.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 13–19, 2 figs. [11 refs.] **II. Survival of *Pseudomonas aeruginosa* within Livers and Spleens of Mice.** *Ibid.*, 20–23.

I. Several workers have shown that bacteria injected into the blood stream are removed from it as rapidly and effectively in animals which have received a moderate dose of whole-body ionizing radiation as in untreated animals (CALLAWAY and KERBY, *Arch. Dermat. & Syph.*, 1951, v. 63, 200; HOLLINGSWORTH and BEESON, *Yale J. Biol. & Med.*, 1955, v. 28, 56; GORDON *et al.*, *Proc. Soc. Exper. Biol. & Med.*, 1955, v. 89, 577). In normal animals the bacteria are retained and destroyed by the phagocytes, whereas in irradiated animals they soon reappear in the circulation and multiply.

The present authors suggest that this is due to an interference with the mechanism by which ingested bacteria are destroyed, though the ability of phagocytic cells to ingest bacteria remains unchanged. To test this hypothesis, peritoneal exudates were induced in mice by the intraperitoneal injection of 15% nutrient gelatin; and the survival, within phagocytes in the exudates, of 10^6 to 10^9 *Pseudomonas pyocyanea* injected 16 hours later was determined in immunized and non-immunized mice, 5 days after exposure to varying doses of X-rays. The immunized mice were given one subcutaneous and four intraperitoneal injections of increasing quantities of a heat-killed suspension of the *Ps. pyocyanea* strain. Determinations of the survival of organisms were carried out by culturing dilutions of ground phagocytes, which had been maintained in media containing bactericidal amounts of polymyxin B to limit determination to intracellular bacteria.

The packed cell volume of phagocytes recovered from the exudates varied inversely with the dose of radiation received by the donor mice and it was found that bacterial survival was highest within phagocytes obtained from non-immunized mice receiving the highest doses of radiation. Phagocytes from immunized mice destroyed intracellular bacteria more effectively than phagocytes from non-immunized mice even though the immunized donor mice had been irradiated.

The authors consider that the ability of phagocytes to kill intracellular bacteria is adversely affected by whole-body irradiation and that the increased digestive capacity of phagocytes following immunization was suggestive of a physiological change at the cellular level.

II. The authors extend their work to the fixed phagocytic cells of liver and spleen. Mice were subjected to varying doses of X-rays and 5 days later were challenged with 4×10^8 viable *Pseudomonas pyocyanea* (1 mouse LD100). This was immediately followed by injection of 1,000 units of polymyxin B intravenously to destroy extracellular bacteria. Livers and spleens from different groups of mice were examined immediately, after 4 hours and after 24 hours. The tissues were ground and the total number of viable organisms was determined by plating out broth dilutions. Frozen sections of liver and spleen removed immediately after inoculation showed that micro-organisms had already been ingested by phagocytic cells.

It was found that bacteria survived and then multiplied in livers and spleens of mice which had received 500–700 r of X-rays but that they were destroyed in the organs of mice receiving only 100–300 r. In the organs of immunized mice the bacteria did not survive even in mice which had been given 500–700 r.

The possible reasons for the greater irradiation resistance of phagocytic cells in organs from immunized mice are discussed briefly. *Max Sussman*

STOLOFF, I. L., HAURANI, F. I., REPPLINGER, Evalyn F. & HAVENS, W. P., Jr. **Effects of Total-Body Irradiation on the Production of Antibody in Man.** *New England J. of Med.* 1959, June 18, v. 260, No. 25, 1258–61, 2 figs.

"The capacity of 7 Schick-negative patients with acute leukemia or disseminated neuroblastoma to respond to a booster dose of diphtheria toxoid after varying doses of radiation and infusion of human bone marrow was determined. Exposure to amounts of radiation ranging from 170 r to 490 r apparently did not significantly alter either the qualitative or the quantitative immunologic response in 5 patients. It is possible that a dosage of 800 r delayed or suppressed the production of antibody, although the data are too meager to cite in support of this. The attempts to demonstrate the transfer of antibody-producing cells from donors to recipients, as manifested by measurable increases in circulating tetanus antitoxin in the recipients, were unsuccessful."

See also p. 1028, SASLAW & CARLISLE, **Effect of Total Body X-Irradiation on the Antibody Response of Monkeys.**

Miscellaneous

SNYDER, J. C. **Ethics and Public Health.** 19 mimeographed pp. 1959. Cambridge: Harvard University, Mass., U.S.A.

The author's thesis is that new knowledge for improving man's health should be fully applied even though the consequences may seem to include the exacerbation of hunger and misery. It is probable that in a few generations our understanding of the human mind will provide far more effective techniques for creating a high order of general education of the whole of society. This is the prerequisite for the prevention of the catastrophic population increase which now threatens to nullify the advances of civilization. Meanwhile the profession of public health must accept responsibility for effective education in matters of health including specifically the information required for regulation of reproduction. To fail to accept this responsibility would be just as wrong as to fail to apply measures for the control and prevention of disease.

Many of man's most useful discoveries and inventions have brought danger and there can be no possible justification for prohibiting exploration in the field of nuclear power. The potential hazards are clearly great, and the responsibilities of public health thereby made correspondingly great, but the benefits of nuclear energy will far outweigh the hazards. *A. Bradford Hill*

Book Reviews

WHITE, Abraham [Ph.D.], HANDLER, Philip [Ph.D.], SMITH, Emil L. [Ph.D.] & STETTEN, DeWitt, Jr. [M.D., Ph.D.]. **Principles of Biochemistry.** 2nd Edition. pp. xiii + 1149, illustrated. 1959. New York. Toronto: McGraw-Hill Book Co. Inc. London: McGraw-Hill Publishing Co. Ltd., McGraw-Hill House, 95 Farringdon Street, E.C.4. [£5 16s 6d.]

That this textbook should appear in a new edition only 5 years after its first appearance is an indication both of the rapid advance of biochemistry and of the concern of the authors and publishers that their book should contain the latest information. It may also partly explain why the book is so expensive: at nearly £6 it is beyond the pockets of many of the private buyers for whom it is designed. However, those who are prepared to pay will possess a very comprehensive, up-to-date, readable and carefully-compiled introduction to all aspects of human biochemistry.

This second edition follows closely the arrangement of the first edition. It consists of 51 chapters divided into 7 parts. The title of the book may be misleading. Only the first 3 parts are really concerned with fundamental principles. The latter sections deal with the specialized biochemistry of man and other mammals, with frequent reference to the biochemical aspects of disease, and to therapy based on this biochemical understanding. This is proper in a work designed primarily as a textbook for medical students, and this aim has been well fulfilled.

The authors assume that their readers have an elementary knowledge of organic chemistry, but little or no physical chemistry. Physical principles are introduced as occasion arises, but the structural chemistry is collected into the first part entitled "Chemical Composition of Cells". These 200 pages might well have been reduced, as they include much material taught under the heading of organic chemistry; some items, such as methods for laboratory synthesis of amino-acids, seem superfluous in a book of this sort.

The second part is a short section dealing generally with enzymes and enzyme action, individual enzymes being discussed in later parts. The next section deals with metabolism. It occupies one-third of the text, and rightly so, for here are the real fundamentals of biochemistry. After a full discussion on biological oxidation, there is the classical division into metabolism of carbohydrates, lipids and proteins. While it is metabolism in man which is primarily discussed, due emphasis is laid on the important contributions made in this field by the study of micro-organisms, plants and animals, and of the fundamental chemical unity among living organisms which is revealed by the study of comparative biochemistry.

Part 4 deals with body fluids, including not only blood, lymph, urine and milk but the many specialized extracellular fluids such as the secretions of the intestinal tract. In Part 5, the biochemistry of the main animal tissues is described—liver, muscle, nervous and connective tissues, bone, eyes and skin. The control system operated by the hormones is discussed fully in Part 6, while the final section on nutrition is mainly concerned with the nature and functions of the vitamins, since many other aspects of nutrition have already been described in other chapters.

There follows an index of 100 pages, double the size of the index in the first edition. This is a further indication of the care with which this work has been prepared. The authors hope that the book will continue to be used as a reference source in the years after its formal use as a textbook. Certainly this index

enhances its value in this respect. Additional aids to easy consultation are the liberal use of cross-references and the well-designed page-headings.

The production of the book is of a high standard. Mistakes are very few. There is liberal use of clear structural formulae and diagrams. References follow each chapter, and are deliberately confined to books and review articles, mostly of very recent date.

C. E. Stickings

ROBERTS, J. A. Fraser [M.A., M.D., D.Sc., F.R.C.P.]. **An Introduction to Medical Genetics.** 2nd edition. pp. x + 263, 107 figs. 1959. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [35s.]

The appearance of a second edition of this book has been awaited with impatience by medical geneticists. The first edition of 1940 has been out of print for so long that even second-hand copies have been unobtainable. The new edition is completely re-written but it must be said at once that the unique features of the book have been retained.

The basic principles of particulate inheritance are explained in a most lucid manner, with examples illustrating segregating traits determined by single genes, entirely drawn from man. The modifications, as at present understood, of patterns of single gene segregations by variation in dominance, in expression, by sex limitation and so on, are clearly set out together with some simple principles applicable to a decision as to a mode of inheritance.

There is a chapter on linkage which explains the first principles in a particularly clear way and another which every student should read on the inheritance of blood groups. In the chapter entitled "The Gene in Action" the modes of expression of genes and the ways in which they are modified are considered in a little more detail than earlier in the book, and the ideas raised should suggest to the imaginative beginner why genetics is a subject of such endless fascination, and should stimulate him to further reading. Chapter X deals with the inheritance of graded or "physiological" differences, which are so influenced in addition by environmental experience, and points to the role of such mechanisms in determining genotypes which are prone to certain common diseases. Again the presentation is simple and stimulating.

The final chapter deals with Genetic Prognosis, setting out the principles of deciding, from available evidence and knowledge, the risks to offspring of a marriage, and the various circumstances of a family history which may modify these risks. No-one is better qualified in this country to write on this subject and it would have been of great interest if this chapter could have been expanded. However, the balance is maintained of introducing the subject as in other sections of the book and sufficient warning is given to the discerning that advice on prognosis should not be given lightly.

So, at last, there is again a book which can be recommended to a medical student or to a qualified man who wants just to understand the elements of human genetics. However, it is the best available introduction for the beginner who wants to go further, because, in spite of its simplicity it covers a great deal of ground and is accurate, so that the reader is properly equipped to read more widely.

Far too many books on genetics purporting to be elementary include pages of algebra and of statistical methodology, much of it extremely interesting as an intellectual exercise, but of little or no relevance to practical problems. Only too often in such books, the phenomena from which the theory is developed are inadequately explained. *An Introduction to Medical Genetics* will be read from cover to cover by many beginners who would be discouraged after the first chapter of some such books. At the end of the reading they will be much wiser than if they had sat with cold compresses round their heads for a very much longer time trying to understand more pretentious volumes. There are many excellent line illustrations and photographs and they are all self-explanatory and properly related to the text. No attempt has been made to give other than key references which is probably a wise decision in view of the size of the literature. The index appears rather compressed but, in practice, its use together with the chapter headings at the front of the book make it easy to find information on any point covered.

Alen C. Stevenson

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